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The order in this section is:—**General; Vital Statistics; Epidemiology; Maternal and Child Health; Health of Students, Nurses and Hospital Staffs; Health of Old Persons and the Chronically Ill; Chronic Cardio-Respiratory Diseases; Chronic Rheumatism; Cancer; Miscellaneous Diseases; Dental Health; Mental Health.**

GENERAL

MINISTRY OF HEALTH. **Report of the Ministry of Health for the Year ended 31st December, 1959. Part I. 1. The National Health Service (including a Chapter on International Health). 2. Welfare, Food and Drugs, Civil Defence.** Cmnd. 1086. pp. xxii + 281. [Refs. in footnotes.] 1960. London: H.M. Stationery Office. [13s.]

This annual report is somewhat smaller than that for 1958 [this *Bulletin*, 1960, v. 35, 2] as the latter included a 10-year survey of the National Health Service. There is a new chapter devoted to the Mental Health Act, 1959, and the one on Prices of Goods Supplied under the National Health Service is now incorporated in the chapter on Medical and Hospital Supplies.

The present report "seeks, where possible, to look ahead by examining trends and new developments, particularly in the important fields of mental health, the geriatric services, the hospital building programme, efficiency in management and good co-ordination between parts of the Service working in the same field."

Finance. The total gross cost of the National Health Service for 1958–59 was £671m. compared with £626m. in the previous year. The hospital and specialist service took £383m. (£357m.); the general medical £66m. (£63m.); the pharmaceutical £69m. (£64m.); the general dental £46m. (£42m.); supplementary ophthalmic £14m. (£14m.) and that of the local health authorities £59m. (£56m.). The figures in brackets are those for 1957–58.

61·9% of the cost of hospitals is for salaries and wages. The national exchequer provided £486m. (£480m.); contributions from the weekly payments levied for the National Health Service on employers and employed £92m. (£57m.); payments by persons using the service £32m. (£32m.); and £28m. (£26m.) came from the rates.

After allowing for the various sources of income the net cost to the exchequer has gone up by only £6m.

The estimated costs for 1959–60 are: gross £640m. and net to the exchequer £501m. but the substitution of a general block grant to local health authorities for a 50% grant has made comparisons unreliable.

Mental Health. The shift of emphasis from institutional to community care is still largely in the planning stage but is being pursued energetically. At the end of 1959 some 9,000 psychiatric patients were being treated on an informal basis in hospitals or parts of hospitals which were not designated as mental hospitals and 34,149 in those that were. Statutory overcrowding in designated mental hospitals decreased from 10·9% to 7·6% during the year.

The new procedures for compulsory detention in hospitals are explained clearly.

Hospitals. The number of available staffed beds fell by 1,500 to 475,000 but the number of completed courses of in-patient treatment increased by 3% to 4,000,275, and those on waiting lists from 443,000 to 476,000. In the medical departments of regional board hospitals an average of 10·8 and in the surgical 23·5 patients were treated in each bed during the year. The number of out-patients treated in all hospitals was over 12 million and they made over 41 million attendances. Home visits paid by consultants numbered 310,062.

At long last the idea that an associated teaching hospital must be within the geographical boundaries of the region it serves has been abandoned and the new Wessex Region, carved out of that of the South West Metropolitan, is still associated with the University of London.

The number of beds occupied by the tuberculous declined by 17% to 14,500. There are now 95 special geriatric units and 30 for the younger chronic sick.

The cost per in-patient week varied between £6 8s. 0d. in mental deficiency hospitals to £34 9s. 5d. in London teaching hospitals.

The most important hospital development has been the provision of more money for hospital building; the amount is now £22m. and is to rise to £31m. in 1961–62.

Resistance to joint contracting for supplies by groups of hospitals is decreasing.

Hospital staffing. There are now 7,102 consultants, an increase during the year of 114: the number of full-time nurses increased by 7,281 to 150,612 and of midwives by 729 to 9,907.

The general medical services. There have been two major trends of policy in recent years: more emphasis on the importance of preventing illness and a switch from institutional to community care wherever possible.

The number of "principals" engaged in the normal service increased by 55 to 19,654, 68·9% of whom practised in partnership. The average number of persons on a doctor's list is 2,282. There are about 15,000 doctors on the obstetric lists.

General dental service. The demand continues to grow and full courses of treatment increased by 4·5% to 10,700,459. 144 more dentists participated in the service and the total is now 10,418.

Supplementary ophthalmic service. The number of sight-tests was 5,306,000 and the number of glasses supplied was 4,585,000.

Pharmaceutical services. The number of prescriptions dispensed increased by just over 10 million to 214,029,087. Most of the increase occurred during the Spring epidemic of influenza. The cost per prescription continues to rise and is now 6s. 9·76d. Proprietary drugs accounted for 77·5% of the ingredient cost. The importance of economy in prescribing is stressed but "it would be a mistake to restrict doctors to a limited range of drugs."

The local authority health services. The total attendances at ante-natal clinics were 1,516,000 and at child welfare clinics 10,201,000; both higher than in 1958. Domiciliary confinements increased by 1,369 to 266,584; this is 37% of all confinements. There was a slight falling-off in the amount of home nursing; 23,565,726 visits being paid to 969,691 patients. The domestic help service continues to expand: the staffs helped 289,500 persons, including 33,245 maternity patients. The health visiting service is also growing and the 7,033 visitors paid 11,951,000 visits.

By the end of 1959 1,632,159 persons had been vaccinated with BCG.

Training centres for the mentally subnormal are being developed rapidly and there are now 424.

Other sections deal with chiropody, vaccination and immunization, the increase of gonorrhoea, health centres, the building programme, the ambulance service and the delegation of health functions to smaller authorities.

Welfare services. At the end of the year there were 94,018 elderly or handicapped persons in residential accommodation: during the year 55 new homes were opened. Many useful hints on how best to provide for the elderly are given.

There were 5,880 persons, including 2,509 children, in temporary accommodation for the homeless. There is an impressive record of what is being done by welfare authorities and voluntary organizations for the handicapped and the aged.

There are chapters on the welfare foods service, food hygiene and civil defence.

The appendices contain 71 pages of statistics.

[The main impression on finishing the reading of this report is to marvel at its immense range and the amount of detail supplied. Though this abstract is long there are many important topics discussed at length in the report of which no mention can be made owing to lack of space.

It is essential reading for all concerned in the executive or administrative work of health services, as is its companion volume, not yet published, the report of the Chief Medical Officer.] *Allen Daley*

JEFFERYS, Margot, BROTHERSTON, J. H. F. & CARTWRIGHT, Ann. **Consumption of Medicines on a Working-Class Housing Estate.** *Brit. J. Preventive & Social Med.* 1960, Apr., v. 14, No. 2, 64–76, 2 figs.

In 1954–55 visits were made to a random sample of $\frac{1}{16}$ of the dwellings in a post-war housing estate (population 17,000) in Hertfordshire to obtain information about the health of the inhabitants and their use of the health services. Adults were questioned at the beginning and end of a 4-week period and 2 further visits were made to households with children. As a result information was obtained about 1,399 adults and 1,056 children (under age 15 years) representing 77% and 87% respectively of adults and children living in the sample dwellings. Further data, relating to general practitioner consultations made in 1953, were obtained for the persons in the sample dwellings (86% of the total) who were registered with practitioners on the estate [this *Bulletin*, 1957, v. 32, 303].

All data relating to the consumption of medicines refers to their use in the 4 weeks between successive interviews. In that period about a quarter of those interviewed had taken prescribed medicines and about two-thirds had taken "non-prescribed" (*i.e.*, obtained without a doctor's prescription). Among children under 10 years of age there was no significant sex difference in either of these proportions, but at older ages consumption of both types of medicines was greater among women than among men; the difference was greatest in the age-group 25–45 years; about 30% of the women compared with 20% of the men in that age-group had taken prescribed and about 80% and 70% respectively had taken non-prescribed medicines. The age and sex groups with high proportions of persons taking prescribed medicines were the same as those with high average rates of general practitioner consultations. A series of informative tables lead to the following conclusions: (1) Children in small families were given more medicines than those in large, and first-born children were given more than those born later. (2) Mothers who had education beyond the minimum of elementary and secondary modern schools gave their children more prescribed and non-prescribed medicines than did other mothers. (3) Wives of black-coated workers gave their children more medicines of both types than did other wives. (4) Mothers who were worried about their own health and those who had "nerves" were more likely to give their children medicine than mothers free from these worries. The most frequently used medicines were laxatives and aspirin and these were almost always non-prescribed. Children in small families were more often given aspirin than those in large families but no such difference was observed for laxatives which appeared to be given as a general routine, and not for specific constipation, to 90% of all children so treated. In this respect the use of laxatives differs with age because 56% of adults taking laxatives reported recent constipation.

Two tables, one for adults and one for children, which cannot be easily summarized, show the diseases for which medication was used, the percentage of cases of each disease for which medicine was taken, the percentage of all medicines taken for each disease which were prescribed, the number of people reporting the disease in the 4-week period and for adults, the type of medicine most frequently taken. *E. A. Cheeseman*

In the review of RAJASTHAN: *Health Statistics 1958* [this *Bulletin*, 1960, v. 35, 330] attention was drawn to an apparent discrepancy between the figures for registered births and the (higher) figures for successful vaccinations of infants. We have now been advised that this discrepancy does not exist, since the numbers of registered births relate to only part of the State (Registration Area), whereas the vaccinations relate to the whole State.

VITAL STATISTICS

COWAN, K. **The Measurement of Community Health.** *Med. Officer.* 1960, Sept. 2, v. 104, No. 10, 151–5.

The author reviews the sources of information that are available for constructing an index of community health—standardized death rates, expectation of life at birth, measurements of morbidity, the survey of sickness, Ministry of Pensions and National Insurance figures, morbidity statistics from general practice, hospital morbidity statistics, cancer registration. Mortality statistics are no longer a true index of the general health of the community since the conditions which, perhaps, have the greatest effect on the wellbeing of the people are not reflected in the death rates. The defects of the morbidity statistics are discussed, the chief is that they do not afford any information as to the trend of disease. The author suggests that the gaps in our knowledge of the ills of the community and the trends of disease in the population could be closed by means of a sampling procedure. A 1% sample survey of every 5 years would show up the current problems of sickness and give a growing and permanent record of disease trends. *W. J. Martin*

LANCASTER, H. O. **Australian Mortality in the Late Nineteenth Century.** *Med. J. Australia.* 1960, July 16, v. 2, No. 3, 84–7, 3 figs. [24 refs.]

The trend of the death rates in Australia differed from those of England and Wales in the early years of registration; infant mortality was only about two-thirds of that in England and Wales and the general death rates were lower up to about age 50. The males in Australia had an excessive death rate compared with the females, due to accidental and violent deaths. A comparison of the mortality experience of the immigrants and the native-born Australians did not produce any explanation for the observed variations in mortality trends. It seems that the immigrants were robust stock and the sub-tropical climate had not produced any physical deterioration in the native-born. Very large annual fluctuations occurred in the death rates: these were due to violent outbreaks of infectious diseases, particularly measles, at irregular intervals. Many of the early workers failed to appreciate that infectious diseases in a sparsely populated country, which could not sustain continued epidemics, did not follow the regular pattern of England and Wales and their importance in contributing to the annual fluctuations in the death rate was overlooked. The excess of urban over rural mortality in Australia in the earlier years was largely due to typhoid fever. *W. J. Martin*

SWAROOP, S. **Introduction to Health Statistics for the Use of Health Officers, Students, Public Health and Social Workers etc.**

This book was reviewed on p. 1072.

EPIDEMIOLOGY

GENERAL REGISTER OFFICE. **Studies on Medical and Population Subjects No. 14. Morbidity Statistics from General Practice Vol. II (Occupation)** [LOGAN, W. P. D.]. pp. vii + 269. 1960. London: H.M. Stationery Office. [25s.]

The data for this survey was collected by about 120 practitioners in 76 practices, in England and Wales, during May 1955 to April 1956. The morbidity experience of the 85,352 males aged 15–64 was analysed by social class and by a further sub-division into socio-economic groups. The 96,727 females were grouped into 18 socio-economic groups; this classification differs from the usual one in that married women were not classified by the husband's occupation but by their own occupation, if they had one, and by their occupational category, *i.e.* working full or part time with or without family responsibilities. The 58,427 children under age 15 were classified by the occupation of the father. An analysis was also made for the 13,724 males over the age of 65 years, of whom one-third were still working.

Some of the conditions showed a gradient with social class or socio-economic groups although in some disorders the relation between occupation and morbidity is

not clear. A broad summary is that non-manual workers had an above average amount of sickness for psychoneurotic and cardiovascular disorders and the manual workers had an excess morbidity from respiratory disorders, gastric disorders, arthritis and rheumatism, and injuries. Agricultural workers had a below average experience. Housewives had an incidence slightly below average but women working full time and also looking after a family had 31% more consultations than the average and the proportion of them consulting was 19% above average. *W. J. Martin*

DENSEN, P. M., BALAMOUTH, Eve & DEARDORFF, Neva R. **Medical Care Plans as a Source of Morbidity Data: the Prevalence of Illness and Associated Volume of Service.** *Milbank Memorial Fund Quarterly*. 1960, Jan., v. 38, No. 1, 48–101, 9 figs. & 1 diagram. [11 refs.]

This report sets out very clearly the methods and results of an analysis of morbidity data contained in the records of a prepaid medical care plan (the Health Insurance Plan of Greater New York). The authors indicate the uses already made of these data in operating the medical care scheme and comment on their potential value in the examination of hypotheses relating to the natural history and epidemiology of disease. The presentation of the data is largely confined to " prevalence rates " for various diagnostic groups during 1948–51, but some more recent data are given. A 10% sample of persons insured in any one complete year of the 4 years 1948, 1949, 1950 or 1951 was used to compute these rates which are, in consequence, based on 60,302 " enrolled years ". For this study " prevalence " is defined as " the number of persons receiving one or more services from a physician for a particular medical condition in the course of a calendar year per 1,000 persons covered in the Plan "; the limitations of this rate are set out in an appendix and a " physician service " is defined as a face-to-face contact between the physician and the patient. Average annual prevalence rates are tabulated for diagnosis, classified according to the 1948 edition of the International Statistical Classification of Diseases, Injuries and Causes of Death, in considerable detail for both sexes combined. For broad diagnostic groups, and for the more important detailed sub-groups, appendices show the average annual prevalence rates for each sex separately and both combined in a series of 8 age-groups.

The 10 broad categories of disease with the highest average annual prevalence rates are shown in a bar diagram for each sex. By far the highest rate for each sex is that for diseases of the respiratory system (420 per 1,000 for men and 424 per 1,000 for women). The next highest rate is 162 per 1,000 for men and 160 per 1,000 for women for diseases of the nervous system and sense organs. In fact, 9 of the 10 broad diagnostic categories with the highest rates are common to both sexes. Diseases of the genito-urinary system ranks 3rd highest for women (128 per 1,000) but is not in the first 10 for men (37 per 1,000). Accidents rank 6th highest for men (110 per 1,000) compared with 8th highest for women (88 per 1,000).

The age specific rates for both sexes combined are summarized in 6 diagrams. Each diagram shows the trend for several diagnostic groups and those with similar age-prevalence trends are shown in the same diagram. For example, one diagram shows the age specific rates for some 15 diagnostic groups for which the rates are highest in childhood and thereafter fall or remain stationary, while another diagram includes some 9 diagnostic groups for which the rates increase to a peak in young adult life and thereafter decrease. The implications of the 6 diagrams are discussed. It is impossible to summarize the wealth of interesting data included in these diagrams; they must be studied in the original where they are supplemented by an appendix giving the actual rates for each sex.

The authors compare their results with those published for the Permanente Health Plan of California by WEISSMAN (*Permanente Foundation Medical Bulletin*, 1951 v. 9, 1) and those for their own scheme in the year 1957–58. The rates from the New York and Californian records were similar for many diagnostic groups, but the New York rates for respiratory disease, arthritis, hypertension and possibly diabetes were higher than those from the Californian scheme. In most diagnostic groups where sufficient stable rates were available from the New York scheme in both 1948–51 and 1957–58, the rates were similar in the two periods but 3 trends were worthy of note—a decrease in the prevalence of skin disease and rheumatism and an increase in that of heart disease appear to have taken place during the decade.

The study concludes with an analysis of the volume of physician services associated with a series of specific diagnostic groups. This analysis is also set out in detail in tables and diagrams which require detailed study, particularly by readers interested in planning health services. In this context it is of interest to note that respiratory diseases, for which the highest prevalence rates were recorded, accounted for about 20% of all physician services and ranked highest on that scale, while the allergic, metabolic, endocrine and nutritional diseases, which were as a group the 7th highest in prevalence, accounted for a further 13% of all physician services and rank 2nd highest on that scale. The authors comment on the age and sex variations in the percentage of all physician services associated with specific diseases and then consider utilization rates (physician services per 1,000 of the population) in similar detail. They conclude that while the utilization rates for a given disease vary with age roughly in the same way as do the prevalence rates, the slopes of the two curves differ because usually the average number of services per case of disease increases as age advances.

In appendices, other than those mentioned above, the methodology is fully described and the completeness of the reporting of the physician services is examined.

[This is a very well presented report with excellent diagrams and in addition the rates on which the diagrams are based are given. An abstract of this length cannot do full justice to the report, which although long, is not verbose—indeed the authors do no more than highlight the important features of their tables and indicate the questions which are raised by them and which such data may help to answer.] *E. A. Cheeseman*

MATERNAL AND CHILD HEALTH

MINISTRY OF HEALTH. **Reports on Public Health and Medical Subjects No. 103. Report on Confidential Enquiries into Maternal Deaths in England and Wales 1955–1957** [WALKER, A. L., WRIGLEY, A. J., ORGANE, G. S. W., CHAMBERLAIN, Roma N. & MARTIN, W. J.]. pp. vii + 60. 1960. London: H.M. Stationery Office. [4s.]

Report No. 97 of this series [this *Bulletin*, 1957, v. 32, 1124] was entitled Report on Confidential Enquiries into Maternal Deaths in England and Wales during 1952–54 and the present report records the findings of investigation continued during 1955–57. In this period there were 2,149,396 births and 1,112 maternal deaths directly due to pregnancy and childbirth. Of these deaths 861 were the subject of enquiry. In addition 339 out of a total of 368 deaths due to disease during pregnancy or childbirth were investigated.

The first section of this Report deals with the history and method of the enquiry which was begun in 1928. This is followed by sections which contain interesting description and numerical data on (1) toxaemia of pregnancy, (2) haemorrhage, (3) pulmonary embolism, (4) abortion, (5) cardiac disease associated with pregnancy, (6) Caesarean section, (7) complications of anaesthesia, (8) sudden death in labour, (9) rupture of uterus, (10) Asian influenza 1957 associated with pregnancy and childbirth, and (11) the "avoidable factors in the whole series", but these factors are also considered in the individual sections. There is an appendix of 8 tables of numerical data.

Toxaemia is still the most important cause of maternal death and accounts for just over one-fifth of the total mortality. The actual number of deaths from toxaemia, which was 246 in the 1952 and 1954 series, was reduced to 188 in the present series but the proportion remains about the same. The percentage of cases of avoidable factors in toxaemia deaths has risen slightly from 52 to 54·8%. It is considered, however, that the proportion of maternal deaths from *all* causes due to avoidable factors has fallen from 43·1 to 40·9%. A substantial proportion of these avoidable factors "is still contributed by the mothers themselves".

This important and valuable Report is clearly presented and should be a great help in identifying the main avoidable factors and hence in taking appropriate action for their elimination. *M. E. Delafield.*

KAUFMANN, H. J. Die Gefährdung Fruhgeborener und Neugeborener durch Medikamente. [**Dangers of Medication in Premature and New-Born Infants**] *Deut. med. Woch.* 1960, June 17, v. 85, No. 25, 1090–93, 1119–20. [65 refs.]

This is a review with no original observations. The author draws attention to the fact that infants have not developed capacity to deal with certain medicaments, so that they cause effects not seen immediately at a later age. The first example cited is Gantrisin (5-sulphanilylamino-3,4,-dimethylisoxazole): this has caused a high mortality, sometimes with kernicterus, and evidence is offered that in the infant there is a greater capillary permeability, permitting the escape of bilirubin into the tissues. The author then reviews recent American literature on fatalities caused in the newborn by overdosage with chloramphenicol, the explanation of which is said to be an incapacity in the newborn for acetylation. Other drugs mentioned as involving special risks at this age are salicylates, corticosteroids, vitamin K, resorcin and aniline dyes. *L. P. Garrod*

HARTMAN, E. E., PARK, W. E. & NELSON, H. G. **The Peeling House Paint Hazard to Children.** *Pub. Health Rep.* Wash. 1960, July, v. 75, No. 7, 623–9.

The occurrence of lead poisoning in small children living in poorly maintained homes in some cities of the United States has been well established [this *Bulletin*, 1956, v. 31, 1059; 1957, v. 32, 302; 1959, v. 34, 785, 849]. The study described in this paper was undertaken to determine whether or not abnormally high urinary lead levels might be found in Minneapolis children even in the absence of lead poisoning symptoms. In Minneapolis no deaths from lead poisoning in small children and no diagnosed cases have been made known to the Health Department for several years.

Between August 25, 1958, and October 10, 1959, a total of 417 specimens of urine from children of 5 years or under were examined for lead concentration by the dithizone method. The high point within the normal range of lead content was taken at 0·08 mgm. of lead per litre.

The findings were: (1) in 199 specimens obtained between August, 1958, and the end of April, 1959, from children attending the well-child clinic 1 was found to contain more than 0·08 mgm., (2) in 194 specimens analysed in the period May to October, 1959, from children attending the clinic 6 were found to contain "high" urinary lead, and (3) among specimens obtained in July to September, 1959, from 24 children living in homes "with badly chipped or peeling paint on the exterior" 9 were found to have abnormally high lead levels.

A full investigation was made of the homes and home conditions with the main conclusions: (1) "The study did not reveal lead hazards to small children in Minneapolis which could be traced to conditions inside of the homes, although the possibility that such hazards exist cannot be completely excluded", (2) "None of the children with high urinary lead manifested sufficient signs or symptoms to warrant a diagnosis of lead poisoning and by late October almost all urinary levels had returned to normal" and (3) "All of the high urinary lead levels appeared during the summer, suggesting a seasonal outdoor exposure and the absence of significant all-year inside exposures". *M. E. Delafield.*

VON HARNACK, G. A. & ONNASCH, C. Wie kommt es zu Vergiftungsunfällen im Kindesalter? Folgerungen für die Prophylaxe. [**Causes of Accidental Poisoning in Childhood**] *Deut. med. Woch.* 1960, Sept. 2, v. 85, No. 36, 1577–80, 1622, 1 fig. [18 refs.]

Accidental poisonings in children have been the subject of a number of published reports [this *Bulletin*, 1957, v. 32, 108 ; 1959, v. 34, 186]. This paper contains an account of an investigation in Hamburg where the incidence of these accidents has risen in the last decades because of the increased use in the home of a variety of washing, cleaning and disinfecting materials and of medicaments.

In the period 1954–58 enquiries from different sources revealed the occurrence of 428 poisonings in children up to 14 years of age and of these a total of 401 cases were analysed. This represents an annual incidence of 3·2 such accidents per 10,000 children or the risk that 1 in 230 children will suffer a poisoning during their childhood. There were 7 deaths due to accidental ingestion of medicated suppositories (3), mushrooms (2), E 605 (1) and strong soda solution (1).

In 343 instances the poisoning was due to the action of the children themselves but in 58 the poisoning was caused by food, overdosage of medicines, administration of the wrong medicines, gas or smoke. Most of the poisonings were in the 2- to 4-year age-group and two-thirds were in boys. The poisoning materials were mainly household poisons (52%) such as turpentine, benzene, paraffin, disinfectants, preservatives, insecticides, alkalis and acids, and medicaments (38·2%) such as barbiturates, belladonna preparations, analgesics and purgatives.

Investigation of 150 families in which poisoning had occurred was carried out. It was found that many of these were in sub-standard homes and that in most of the families the poison had been left readily accessible to the children.

There is a full description of the measures which should be taken to prevent these poisonings and also a comparison of the experiences in Hamburg with those recorded in the literature of other countries.

M. E. Delafield

HEALTH OF STUDENTS, NURSES AND HOSPITAL STAFFS

BARR, A. **Sickness Absence among Hospital Nurses.** *Brit. J. Preventive & Social Med.* 1960, Apr., v. 14, No. 2, 89–98, 2 figs.

This paper is a summary of a detailed analysis of all absences by student, trained and other nurses and nursing assistants in 103 hospitals with about 15,000 beds. The hospitals were administered by the United Oxford Hospitals and Oxford Regional Hospital Board and the data relate to 6,232 nurses (732 males and 5,500 females) in the 12 months ending March 31, 1957. In that period there were 5,309 absences due to sickness (85·2% of the total) which involved a loss of 68,536 days. It is pointed out that this volume of sickness absence " is equivalent to some 190 full-time staff or an annual outlay of between £60,000 and £70,000 ". Most of this paper [and the rest of this abstract] relates to female nurses only ; they had 4,803 of all the spells of sickness absence.

Irrespective of age and residence (*i.e.*, whether the nurse was a resident or non-resident) inception rates (spells) were highest for nursing assistants (110 spells starting in the year per 100 nurses exposed to risk, *i.e.*, 110%) and lowest for trained nurses (64%), while the rates for student nurses (97%) and other nurses (105%) were relatively high compared with trained nurses. In each grade and most age-groups the rates for non-residents were higher than those for residents. Of the trained nurses 57·0% had no sickness absence during the year compared with 38·6% of the student and 38·2% of the other nurses (including assistants). For all grades combined this proportion increased with age (excluding the under 20 years group) from 36·2% at ages 20–24 to about 50% at ages over 40 years. The general trend of the inception rates was to decrease with age, from 102·5% at 20–24 to 75·5% at 55–59, while that of the average duration of absence was to increase from 9·3 days at 20–24 to 18·5 days at 55–59 years. A table shows the causes of sickness absence, the percentage of all spells of absence and the percentage of all days lost attributed to each cause. Age specific inception rates are tabulated for selected causes. The most common cause of absence was the common cold (17·3% of all absences and 6·1% of all days lost). Sinusitis, tonsillitis and other nose and throat conditions accounted for a further 10·2% of spells and 7·6% of days lost.

This paper includes comparisons between the Oxford nurses and appropriate sub-groups of the sickness absence data published by the London Transport Executive and by the Ministry of Pensions and National Insurance. These comparisons suggest that infectious, circulatory and skin diseases were more common among the Oxford nurses than might be expected. An examination of the variation between hospitals in the Oxford area showed that although no important differences were found in inception rates there were significant differences in the average durations of absence. The author suggests further investigation of these hospital differences and the high rates for infectious, circulatory and skin disorders and recommends a review of the residential accommodation provided for the young student nurse. To achieve such ends, and to facilitate further research into the uses of sickness absence data, standardized methods of recording absences of hospital nursing staff is advised.

E. A. Cheeseman

HEALTH OF OLD PERSONS AND THE CHRONICALLY ILL

TOWNSEND, P. **Social Surveys of Old Age in Great Britain, 1945–58.** *Bull. World Health Organization.* Geneva. 1959, v. 21, Nos. 4/5, 583–91. [12 refs.]

In this paper the author summarizes the most important findings produced by 33 social surveys of old age which have been carried out in Great Britain since the Second World War. He points out that concern with the social, economic and medical problems of the aged in the community has largely replaced the pre-war interest of research workers in unemployment and in malnutrition among children.

The surveys reviewed in this paper were all concerned with old people living in their own homes. Contrary to popular belief, they showed that the great majority of those in their seventies or eighties have frequent contact with and help from their younger relatives. The author suggests, however, that there were three groups whose needs were often unmet and whose consequent suffering was great. There were, firstly, the "house-bound" and particularly the "bed-fast" who constitute approximately 8% and 2% respectively of the population of pensionable age. Secondly, there were those who had not married or were childless and who had no surviving kin. About 25% of the age-group fell into such a category and many of them were lonely and neglected. The third group was composed of men for whom retirement from poorly paid wage-earning jobs meant both savage economic stringency and loss of standing among their workmates and family circle.

The author suggests that, in the future, priority needs to be given to improving the means of locating those in need, to providing isolated people with substitute social relationships and to easing the transition from work to complete occupational retirement by the institution of a "running-down" period to coincide with declining capacity for work. *Margot Jefferys*

CHRONIC CARDIO-RESPIRATORY DISEASES

ENTERLINE, P. E., RIKLI, A. E., SAUER, H. I. & HYMAN, M. **Death Rates for Coronary Heart Disease in Metropolitan and Other Areas.** *Pub. Health Rep.* Wash. 1960, Aug., v. 75, No. 8, 759–66, 2 figs. [12 refs.]

A comparison has been made of the death rates for people aged 45–64 during 1949–51 for the whole of the United States by density areas—metropolitan areas, containing at least one city with 50,000 or more persons, and non-metropolitan areas. The metropolitan areas have been subdivided into centre city counties and suburban counties; the counties were defined without regard to state boundaries.

Coronary heart disease and all other cardiovascular diseases showed a progression with urbanization for both males and females. The non-metropolitan counties had a death rate from coronary disease of about two-thirds that of the centre city counties, and suburban counties had an intermediate rate. The death rate from all causes less cardiovascular diseases also showed a progression with density of population. Some exceptions to the general trend occurred and in a few areas the non-metropolitan areas had the large rate. There was a distinct geographical distribution of mortality and high death rates were recorded on the South Atlantic coast, north-eastern and Great Lakes region, Mississippi River Delta region and in the area west of the Rockies.

W. J. Martin

SCHROEDER, H. A. **Relation between Mortality from Cardiovascular Disease and Treated Water Supplies. Variations in States and 163 Largest Municipalities of the United States.** *J. Amer. Med. Ass.* 1960, Apr. 23, v. 172, No. 17, 1902–8. [10 refs.]

In 1950–51 a United States Geological Survey analysed the quality and constituents of water supplies of 1,315 cities in the U.S.A. It was estimated that these supplies served 90% of the urban and 58·3% of the rural population in the 49 states. Two tables are given which show for each state the weighted (by population served) average hardness of the water supplied and age adjusted (direct standardization) mortality rates from all causes, from all causes except cardiovascular disease, from all cardiovascular disease, coronary heart disease, and all cardiovascular disease except coronary heart disease. The first table relates to all ages of the total population except that for the last two cause-of-death groups only males are considered. The second table is confined to white males aged 45–64 years. In both tables average annual mortality rates in 1949–51 are shown.

Correlation coefficients (r) were calculated between the water hardness variable on the one hand and each of the mortality variables on the other. The values of r were small and non-significant at $P=0{\cdot}05$ with mortality attributed to causes other than cardiovascular. All the other correlations (*i.e.* those with cardiovascular disease mortality) were significant and ranged from $-0{\cdot}3$ to $-0{\cdot}6$, suggesting that, on average, states with hard water had low mortality rates from cardiovascular disease while states with soft water had high rates from such disease.

These results were confirmed, although not tabulated in such detail, by a similar analysis for 163 metropolitan areas of the U.S.A. For this confirmation death rates from coronary heart disease in white males aged 45–64 years were used. With these data correlations were also calculated between mortality and about 20 other characteristics or constituents of the water supplies. Significant negative correlations ranging from $-0{\cdot}2$ to $-0{\cdot}3$ were found with content of magnesium, calcium, bicarbonate, sulphate, fluoride and dissolved solids. It is stated that when the effect of hardness was removed [presumably by

partial correlation methods] the significant correlations disappeared, which implies that there was no factor in the effect of hardness not explained by the other characteristics. Further, the mortality was significantly correlated with the specific conductivity of the water (−0·21) and its *p*H (−0·20).

It is concluded that while the meaning of these relationships is not yet clear the analysis permits three speculations. "1. There is something 'beneficial' to the outcome of cardiovascular disease in hard waters. 2. There is some adverse factor in soft waters. . . . 3. Soft waters and acid waters attack the pipes through which they run, taking up zinc, cadmium, iron, copper or lead, depending on the kind of pipes and solders used. In that event, cadmium or lead might be suspect; both accumulate in human tissues."

[Although the correlation coefficients on which these speculations are based are significant, those involving the constituents of the water are particularly small; consequently an extension of this work, in which other possible environmental factors are considered, is opportune so that the relative contributions of such factors may be more precisely assessed. As the author modestly suggests, his data "offer a clue" to one environmental factor.] *E. A. Cheeseman*

AMERICAN J. PUB. HEALTH. 1960, Mar., v. 50, No. 3, Pt. 2, 34 pp., 7 figs. [Numerous refs.] **Prevention and Control of Heart Disease. A Symposium.**

This special publication contains five papers presented at a symposium on the prevention and control of heart disease held, in October, 1959, by the American Public Health Association. Reports of two contributions to the discussion and a summary are also included.

J. A. BÖÖK (pp. 1–4) made some general introductory remarks about genetical studies and considered two specific topics, congenital cardiac malformations and hyperlipaemia. Although the incidence of cardiac malformations in sibs of affected persons has been estimated at 1·4–1·8% and although for a few specific clinical entities more precise estimates have been made, it was impossible to make any precise definition of the genetic role in the aetiology because of the heterogeneity of the available data. Böök felt that future genetic studies would be unrewarding until more was known about the pathogenesis, pathophysiology and embryology of cardiac malformations.

It has been demonstrated that a simple dietary regime reduces the concentration of cholesterol and neutral fats in the serum of persons who are heterozygous for genetic hyperlipaemia and it will be of interest to see if this affects the subsequent incidence of coronary disease or other atherosclerosis in such persons who, in the past, have been characterized by the appearance of such disease in early adult life.

J. MAYER (pp. 5–10) reviewed an extensive literature on nutrition and heart disease emphasizing the difficulties of interpreting the available data and the possible interaction of suspected aetiological factors such as obesity and physical activity. This speaker commented on the fact that so little work had been done on the problems of regulating blood cholesterol and raised several specific questions which should be answered.

E. D. FREIS (pp. 11–13) referred to an unpublished study of the use of anti-hypertensive drugs which indicated that a non-toxic compound of available drugs reduced the average diastolic blood pressure of a large number of hypertensive patients to below 90 mm. Hg. The question of whether or not high arterial pressure is in itself harmful now has new significance and he felt that the evidence was more often in favour than against the hypothesis that the elevation of blood pressure was a major cause of cardiovascular damage in hypertension.

J. STAMLER (pp. 14–19) reviewed the work done by pathologists, clinicians, biochemists and epidemiologists in support of the thesis that raised blood cholesterol is a significant factor in the pathogenesis of atherosclerosis. He described the principal results of a large number of studies and underlined the multiplicity of factors which have been implicated. He suggested that data now available from the Framingham study made it possible to assess fairly precisely the influences of hypercholesterolaemia, hypertension and obesity; middle-aged men who were "normal" in respect of all these factors had an average annual incidence rate of 2·5 per 1,000 for coronary heart disease compared with 36 per 1,000 among men who were "abnormal" with respect to two or all of these factors. He suggested that "high risk, coronary prone, susceptible persons" could be identified before clinical manifestation of coronary disease by means of a set of simple medical determinations, "the measurement of weight, blood pressure, serum cholesterol, thyroid function, carbohydrate metabolism; the assessment of kidney status, family history, smoking status, physical activity status. Except for sex and heredity, all the findings associated with increased risk of coronary disease are generally amenable to correction and/or control by simple, safe means. Nutrition is a cornerstone of these corrective measures."

E. C. HAMMOND (pp. 20–26) described the work done on the association between smoking and heart disease in different parts of the world and he summarized the results of the major study in which he was personally concerned [HAMMOND and HORN, this *Bulletin*, 1958, v. 33, 753]. He pointed out that the explanation for the observed association between coronary heart disease and cigarette smoking must take into account the results of such enquiries. *i.e.*, that "(1) cigarette smokers as a group have higher death rates from coronary artery disease than do non-smokers; (2) the coronary artery disease death rate increases with degree of exposure to cigarette smoke; and (3) among persons who have smoked cigarettes for many years, the death rate is lower for those who have stopped smoking for a year or longer than for those who continue to smoke cigarettes." He considered alternative hypotheses but found it hard not to believe that cigarette smoking increased the mortality rate from coronary heart disease.

Jessie MARMORSTON (in discussion) described experiments carried out during the last 6 years on the relationship between atherosclerosis and the endocrine glands which have included studies of blood lipids and hormonal excretion levels of many patients (pp. 27–28). Some results were given and it was concluded that hormones may play a significant part in atherosclerosis and its complications.

D. D. REID (pp. 29–30) discussed most of the contributions to the symposium and concluded: "The epidemiological evidence is still not quite strong enough to incriminate any particular agent as the major determinant of coronary disease. The verdict must be that very canny Scots one of 'non-proven'. But if I had to hazard a guess, my bet would be that the most readily alterable and important environmental factor in ischemic heart disease is cigarette smoking."

I. S. WRIGHT summarized the symposium by dealing critically with selected topics raised by the previous speakers and concluded with some statistics indicating the importance of these diseases and the size of the problem in the modern world. *E. A. Cheeseman*

CANCER

STOCKS, P. & DAVIES, R. I. **Epidemiological Evidence from Chemical and Spectrographic Analyses that Soil is concerned in the Causation of Cancer.** *Brit. J. Cancer.* 1960, Mar. v. 14, No. 1, 8–22. [10 refs.]

Samples of soil have been collected from the gardens of houses in North Wales and Cheshire where a death occurred from cancer of the stomach, intestine, rectum, larynx, lung or breast or from leukaemia or Hodgkin's disease. Control samples were obtained by selecting addresses of houses in which persons had died from causes other than cancer and matching as nearly as possible the sex, age and district of residence of the person who had died from a cause other than cancer with that of a person who had died of gastric cancer.

The area studied included the 55 administrative districts in North Wales and 11 districts in Cheshire, excluding county boroughs. In this area the death rate from stomach cancer was high and in 1947–55 the standardized mortality ratios for the districts ranged from 65 to 262 compared with 100 for all England and Wales. Estimates of the amount of organic matter present in the soils by two methods (described as showing (i) the amount of organic carbon present and (ii) the loss on ignition) showed a fairly high correlation between the mean values and the standardized mortality ratio (SMR) from stomach cancer for 9 groups of districts. The soil data for the non-cancer control series gave correlation coefficients of 0·466 and 0·569; the soil data for the series of patients with cancer, other than gastric cancer, gave coefficients of 0·402 and 0·503.

Comparison of the organic content of the soil taken from gastric cancer, other cancer and non-cancer houses showed differences according to (i) whether the area was one with a normal or a high mortality from gastric cancer and (ii) how long the subject had resided in the house. For districts with a SMR for gastric cancer less than 150, there was little difference between the gastric cancer and the other soils, but there was a slight excess of gastric cancer cases where the soil had a high content of organic matter (organic carbon more than 5%; ignition loss more than 11·5%). For districts with a SMR of 150 or more, there was a substantial excess of gastric cancer cases where the soil had a moderate or high organic content. In houses where the subject had been resident for less than 20 years the greatest excess corresponded to soils with an organic carbon content of more than 5% (ignition loss of more than 14·5%), but in houses where the subject had been resident for more than 20 years, the greatest excess occurred with moderate values (2 to 3·5% organic carbon, 11·5 to 14·5% ignition loss). Similar results were obtained in a small series of gastric cancer and control soils from two townships in Devonshire. The mean content of organic matter was higher in the township with the higher gastric cancer mortality and was higher in the gastric cancer soils than in the control soils.

Measurements were also made of the amounts of zinc, cobalt, nickel, chromium, vanadium, titanium, iron and lead in soils removed from gastric cancer, other cancer and non-cancer houses in North Wales and Cheshire and from gastric cancer and control houses in the two Devonshire townships. In all three districts the zinc content was higher in the gastric cancer than in the control soils, but there was no correlation between the zinc content of the soil and the total gastric cancer mortality in the area. Similar associations were found between gastric cancer and the cobalt and chromium content of the soils and a positive association was also found between the chromium content of the soil and intestinal cancer. The results obtained from the other metals were inconclusive.

There is no evident explanation for these findings; in the authors' opinion they suggest that aetiological role of vegetables, water supply, air pollution and radioactivity should be investigated. *Richard Doll*

ALLEN-PRICE, E. D. **Uneven Distribution of Cancer in West Devon, with particular reference to the Divers Water-Supplies.** *Lancet.* 1960, June 4, 1235–8, 2 figs.

Examination of the cancer mortality in West Devon during the period 1939–58 shows a great variation in the crude cancer death rate recorded in the different parishes. Parishes with the highest mortality are mostly situated in areas where the geological formation is Devonian and highly mineralized, whereas parishes with the lowest mortalities are situated in areas, described geologically as carboniferous. It is suggested that the differences in cancer mortality may be accounted for by differences in the water supplied to the parishes. Notable differences in cancer mortality are observed within one parish which has been formed out of parts of four others and which obtains its water from three different sources. A high cancer mortality is recorded in that part which obtains its water from a source in another parish which has a

high cancer mortality; a low mortality is recorded in the part which obtains its water from springs and an intermediate mortality, similar to that of Plymouth, is recorded in the part supplied by the Plymouth corporation. *Richard Doll*

RAASCHOU-NIELSEN, Elisabeth. **Smoking Habits in Twins.** *Danish Med. Bull.* 1960, June, v. 7, No. 3, 82–8, 1 fig. [12 refs.]

Information is being collected about all twins born in Denmark during the years 1870–1910. So far 17,600 pairs have been listed and, of these, 4,700 pairs have been fully investigated. For the present inquiry, twins have been excluded: (1) if they were of different sex, (2) if either was dead, resident abroad or an inmate of a mental institution, or (3) if either had failed to cooperate in a previous study. A questionnaire about smoking habits was sent to the remaining 1,240 pairs of twins and useful information was obtained for 894 pairs. This sample was found to be representative of the total with regard to sex, age, zygosity and place of residence.

Information about zygosity had previously been obtained by means of another questionnaire; this was shown to be reliable by comparing the results in a subsample with those obtained by blood grouping. The record of the smoking habit was also shown to be reliable by personal interviews with a sub-sample of 50 pairs chosen at random. By the use of a similar technique and by comparing the results with those obtained in the national survey of smoking habits it was possible to conclude that the results were representative of the smoking habits of all living twins in Denmark.

The results showed that there was greater concordance of smoking habits—both with regard to amount smoked and to method of smoking—among monozygous than among dizygous twins. Concordance was, however, not complete. On average the amount of discordance with regard to smoking or non-smoking in monozygous twins was about half that expected if concordance had been determined solely by chance. In a series of 12 monozygous pairs of twins that had been brought up apart, the amount of concordance was the same as that observed in monozygotic twins in the present study. It is concluded that both genetic and environmental factors play a part in the formation of smoking habits.

The data are as yet too small to distinguish between the effects of genetic factors and of smoking habits *per se* in the development of disease.

[The results of this model study are unequivocal. For purposes of follow-up the numbers are small so that not many lung cancers will be observed, but they should provide conclusive evidence of the relative importance of constitution and of tobacco in the aetiology of the more common diseases.] *Richard Doll*

KOBASHI, Y., SAKAGUCHI, S. & IZAWA, M. **Combustion Temperatures of some Unblended Cigarettes and the Transfer of Nicotine into Cigarette Smoke.** *Bull. Agric. Chem. Soc. of Japan.* 1960, May, v. 24, No. 3, 274–7. [Refs. in footnotes.]

CHATGIDAKIS, C. B. **The Incidence of Malignant Disease in 1,620 African (Bantu) Gold Miners. An Autopsy Survey.** *Arch. Environment. Health.* Chicago. 1960, July, v. 1, No. 1, 17–19.

"The autopsy incidence of malignant disease in 1,620 African male gold miners was found to be 6·3%.

"Primary carcinoma of the liver was the commonest type found, 72% of all malignancies.

"The over-all incidence of primary lung cancer was 0·3% and formed 4% of all malignancies.

"No evidence of an increased incidence of primary carcinoma of the lung was found in African gold miners."

MISCELLANEOUS DISEASES

WORLD HEALTH ORGANIZATION: MONOGRAPH SERIES No. 44. 471 pp., numerous figs. [Numerous refs.] **Endemic Goitre.** 1960. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [40s.; $8.00; Sw.fr. 24.–.]

This volume in the Monograph Series of the World Health Organization contains 12 reviews prepared by "well-known goitre workers" to cover all aspects of the subject of goitre and its control. It includes the 6 chapters published in a special issue of the WHO *Bulletin* (1958) now revised and brought up to date by the authors.

History of Goitre by P. LANGER (Czechoslovakia), pp. 1–25. This is a scholarly article in which the history of goitre is traced from about 3,000 B.C. when the disease was described in Chinese literature, through the Middle Ages, the Renaissance and after to the gradual development of knowledge of the anatomy and physiology of the thyroid, the introduction of iodine treatment of goitre in the early 19th century and the first large-scale trials of iodine prophylaxis in the early 20th century.

Prevalence and Geographical Distribution of Endemic Goitre by F. C. KELLY and W. W. SNEDDEN (England), pp. 27–233. This paper from the Chilean Iodine Educational Bureau, London, shows in detail that goitre occurs with varying intensity in almost every country. There is a wealth of description with numerical data, tables and maps based on the extensive list of references classified by country of origin.

Health Significance of Endemic Goitre and Related Conditions by F. W. CLEMENTS (Australia), pp. 235–260. The natural history of endemic goitre in affected persons is described in sections on the enlargement process, variations in prevalence in children by locality and secular trends and sequelae of colloid goitre in children and in adults. In the second part of the paper there is description and discussion of sequelae in the progeny of goitrous parents—cretinism of a number of defined types, deaf-mutism and mental deficiency.

Physiology of Endemic Goitre by J. B. STANBURY (U.S.A.), pp. 261–277. This chapter contains a clear, brief account of the physiology of the thyroid and of the metabolic circuit of iodine, followed by a review of the information which is available regarding the functional abnormalities of the human gland when it is deprived of iodine.

The Study of Experimental Goitre by S. MILCU (Rumania), pp. 279–313. Much experimental work has been done on the complex mechanisms concerned in the goitrogenic process and this is reviewed with particular accounts of the author's animal experiments. The findings of these are described with tables, figures and photographs. Particular emphasis is placed on the concept of endogenous defect of the thyroid, the causes of which are manifold. "Among them our studies have shown the role of the nervous system, of certain hormones, and of thyroid immunopathology."

Pathological Anatomy of Endemic Goitre by M. P. DE SMET (Belgian Congo), pp. 315–349. This is a review of the pathological appearances of the different types and phases of the goitrous process with a section on classifications of endemic goitre. The selection of a classification must depend on whether it is needed for medical surveys, for clinical use or by the pathologist for descriptive purposes.

Etiology of Endemic Goitre by J. ROCHE and S. LISSITZKY (France), pp. 351–368. Some general comments on the mechanism by which goitre is produced are followed by consideration of "on the one hand, the evidence for the view that iodine deficiency is an important factor in endemic goitre and, on the other, the evidence that its importance is limited". The authors next review the literature on the nature and mechanism of antithyroid substances, experimental study of dietary goitrogens, observations on the relation of dietary goitrogens and endemic goitre, indirect nutritional factors and non-nutritional factors.

Technique of Endemic Goitre Surveys by C. PEREZ (Guatemala), N. S. SCRIMSHAW (U.S.A.) and J. A. MUÑOZ (Basutoland), pp. 369–383. The authors state that "This chapter has been planned for the specific guidance of the physician who wishes to carry out surveys to determine the prevalence of endemic goitre in a population". Separate sections give information on methods employed in goitre surveys, significance of non-visible goitre, assessment of size of gland, technique of examination, classification of goitres, organization of survey, selection of sample, tabulation and presentation of survey data, and observations to supplement the surveys.

Therapy and Prophylaxis of Endemic Goitre by J. MATOVINOVIC (U.S.A.) and V. RAMALINGASWAMI (India), pp. 385–410. An outline of the history of iodine therapy, iodine prophylaxis and of the treatment of goitre by thyroid preparations and by surgery, introduces a review of the present-day therapy of endemic goitre in which there are sections on iodism, Jod-Basedow, iodine thyroiditis and the enlargement of the thyroid which may occur when massive doses of iodine are given in the treatment of various diseases. This is followed by consideration of the modern prophylaxis of endemic goitre, dosage of iodide or iodate, indications for general prophylaxis and recent work in Switzerland and Central America.

Iodized Salt by J. C. M. HOLMAN (London) and W. MCCARTNEY (London), pp. 411–441. This chapter by officers of the Chilean Iodine Educational Bureau, London, contains much detailed technical and other information with a number of illustrations on the extraction and refining of salt, and on a number of methods used in different countries in the production of iodized salt of various types. There is also consideration of the levels of iodization which have been adopted in different countries and also of techniques for the determination of iodine in iodized salt.

Principles and Problems of Endemic Goitre Control by F. W. LOWENSTEIN (Switzerland), pp. 443–452. The main topics considered in this short chapter are (1) objections to the use of iodized salt which have been put forward, (2) administrative problems, (3) international collaboration in the study of goitre and (4) outstanding problems.

Legislation on Iodine Prophylaxis by J. DE MOERLOOSE (Switzerland), pp. 453–462, ends with a list of legal enactments in many countries. The author reviews the legislation on compulsory administration of iodized salt, levels of iodization, control of iodization, the packing and labelling of iodized salt, and provisions relating to technical and financial assistance. *M. E. Delafield*

COSTA, A. & MORTARA, M. **A Review of Recent Studies of Goitre in Italy.** *Bull. World Health Organization.* Geneva. 1960, v. 22, No. 5, 493–502. [Numerous refs.]

This is an interesting review of the Italian literature since 1940 on goitre in Italy. In that year, epidemic goitre appeared in the Alps and the Piedmont plain. It affected thousands of troops assembled in Cuneo Province, a persistent endemic goitre area, and later spread to thousands of civilians in the other Piedmontese provinces. The epidemic disappeared in 1945 and new smaller foci developed in other parts of Italy until 1948. There is a summarized account of the characters of this epidemic goitre, its symptomatology, its seasonal increase in the summer, its occurrence in dogs, and the experience that administration of iodine had no prophylactic value nor did it cause regression of the disease.

The literature on endemic goitre is also reviewed and gives the impression that its prevalence in southern Italy has increased. A description is given of the results of recent field and laboratory researches on thyroid function; thyroid cretinism and deaf-mutism; and the endemic environment.

Among the conclusions it is stated: "As to features favouring an endemic situation, it does not appear that food factors are to be incriminated in Italy, either as being possibly goitrogenous or as being deficient in iodine. Where measurements of the iodine in drinking-water and of the urinary excretion of iodine have been made, no substantial differences between endemic areas and non-endemic areas have been brought to light."

M. E. Delafield

Sanitation

The order in this section is:—**General; Water and Swimming Baths; Sewage, Trade Waste and Refuse Disposal; Housing; Infestation; Atmospheric Pollution; Port, Ship and Aviation Hygiene.**

WATER AND SWIMMING BATHS

(Including the Bacteriology of Water Supplies)

SCHMIDT, B. Bakteriologische Untersuchungen zur Frage der Verwendbarkeit von Polystyrol-Erzeugnissen in Trinkwasserleitungen. [**The Use of Polystyrol Products in Drinking Water Pipes. Bacteriological Investigations**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 178, No. 3, 381–92. [16 refs.]

A short review of the literature on the use of various plastic materials for drinking-water pipes introduces the work described in this paper. The object of this investigation was to determine whether the use of polystyrol for the manufacture of apparatus employed in the laboratory for the measurement of bacterial numbers might have the effect of increasing bacterial counts by causing multiplication of the organisms. The experiments carried out are fully described. They consisted of (1) comparison of bacterial counts in mains water with and without addition of polystyrol in granular form, (2) similar comparison in mains water inoculated with haemolytic *Staphylococcus aureus* or with *Escherichia coli*, and (3) comparison of counts in Söhngen solution (NH_4Cl, K_2HPO_4 and $MgSO_4$ in distilled water) inoculated either with the same organisms as in (2) or also with typical water bacteria with and without polystyrol. The experiments were carried out at 4°C., 20°C. and 37°C.

The results of the experiments do not provide any evidence that polystyrol has any effect on bacterial counts by acting as an additional nutrient for the organisms. *M. E. Delafield*

SCHYMA, D. Anreicherung von Bakterien aus dem Wasser mit einem löslichen Ultrafilter. [**The Concentration of Bacteria suspended in Water with the help of a Soluble Ultra-Filter**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 178, No. 2, 229–36, 2 figs.

A method is described for the preparation of a soluble aluminium alginate membrane filter suitable for use in the bacteriological examination of water. The starting material is a commercial sodium alginate powder "Protanal HF". 10 gm. of this powder added to 990 ml. of distilled water and left overnight gives a viscous yellow fluid which can be stored in the refrigerator for 4 weeks. A thin layer of this solution is spread mechanically to a depth of 0·7 mm. on the surface of a sheet of filter-paper, of appropriate size, previously soaked in a molar solution of aluminium chloride. After 1½ minutes the gel formed on the filter-paper surface is washed in water, autoclaved between two sheets of filter-paper and kept under water until required.

The alginate membrane formed in this way is a water-clear gel in a sheet of thickness 0·5 mm. It is composed of two distinct zones, a primary gel membrane 20μ in thickness, which is the effective filtering component, and a secondary supporting zone containing capillary channels of diameter 20–25 μ which run at right angles to the primary membrane.

The membrane is completely impermeable to bacteria, and also holds back colloidal gold particles of only 20 mμ in diameter. Water is filtered through it under slight negative pressure. The membrane is then dissolved by immersing it in a solution of 3·8% neutral sodium citrate solution, which was shown to be quite innocuous to bacteria and even to tissue cultures. *B. Moore*

RAMADAN, F. M. **Comparative Studies on the Detection of Pollution of Water, Milk, and Ice Cream.** *Applied Microbiol.* Baltimore. 1960, July, v. 8, No. 4, 199–204. [32 refs.]

The frequency of isolation of faecal streptococci by the method of COOPER and RAMADAN [this *Bulletin*, 1955, v. 30, 814] was compared with the coliform test on 122 water samples, 205 milk samples and 58 ice-cream samples. The streptococcus test was carried out in all cases on 10 ml. samples, water samples were examined for coliforms by the standard Ministry of Health method [presumably on 100 ml. samples], and milk and ice cream on 1 ml. of a 1 in 100 dilution only. Coliforms were detected in 5% of water samples, 4·4% of pasteurized milk samples, 1·1% of raw milk samples and 1·7% of ice-cream samples. Corresponding results for streptococci were 17·2, 35·4, 47·8 and 36·2% respectively. The discrepancy in the water samples was mainly seen in those after chlorination, indicating a high tolerance of streptococci to chlorination. The streptococcal index is suggested as a better safeguard for control of pathogens known to resist chlorination.

The high discrepancy between the two indicators in the results for milk and ice cream could be accounted for largely by the great difference in size of inocula used—10 ml. as against 0·01 ml. respectively, but resistance of streptococci to pasteurization and multiplication within milk and ice-cream plants are also given as explanations of the difference. The value of the streptococcal index would depend on further information outlining differences between direct pollution and continuing growth in the processing plants. *E. Windle Taylor*

See also p. 1159, SCHROEDER, **Relation between Mortality from Cardiovascular Disease and Treated Water Supplies. Variations in States and 163 Largest Municipalities of the United States.**

HOUSING

DEPT. SCIENT. & INDUST. RES. Building Res. Station. **Densities in Housing Areas** [STEVENS, P. H. M.]. *Tropical Building Studies No. 1.* 1960, 55 pp., 3 figs. (1 folding). [16 refs.] London: H.M. Stationery Office. [10s.]

This paper sets out the principles governing the planning of housing densities in the physical and social development of communities. In any given area, the population densities that can be achieved by various methods, proportion of land built on, building high or low, etc., are calculable mathematically: the principles are by no means as obvious as they might seem. Although high housing densities are not necessarily less desirable than low densities, naturally the most difficult problem, and main preoccupation of the paper, is the combination of high density with a reasonable degree of social amenity. From this viewpoint the *floor space rate* (the ratio of total floor space to inhabitants) is of obvious importance, but where conditions enforce low floor space rates the *total living space rate* (defined as the ratio of total uncovered area in the house group plus the total floor space to inhabitants) is even more important. The latter is, in the author's opinion, "perhaps the most significant aspect of housing density". No marked increase in density can be achieved by higher buildings until the ratio of the total living space rate to the floor space rate drops to 3·75 : 1 or less.

The whole subject emerges as being of a surprising complexity, and this succinct and lucid exposition is strongly recommended to everyone concerned with the planning of housing. Tables and graphs are given, for the calculation of the various factors involved in housing densities. *B. B. Waddy*

INFESTATION

HAYES, W. J., Jr., MATTSON, A. M., SHORT, J. G. & WITTER, R. F. **Safety of Malathion Dusting Powder for Louse Control.** *Bull. World Health Organization.* Geneva. 1960, v. 22, No. 5, 503–14, 2 figs. [13 refs.]

Because of the existence in some parts of the world of strains of lice resistant to DDT and gamma BHC, there is a need for other chemicals of low toxicity to man which will kill lice. The organic phosphorus compound malathion, which is effective for louse control, has been shown in several published papers to be a safe insecticide in human exposure studies.

The investigation described in this paper was carried out because no work had as yet been done on the effect of prolonged dermal applications of powders containing high concentrations of malathion. In these experiments the bodies and clothing of human volunteers (39) were dusted 5 times a week for 8–16 weeks with talcum powder containing 0, 1%, 5% and 10% of malathion. Blood cholinesterase levels and urinary excretion of malathion-derived material were determined in the spring and summer months.

The results of these analyses and the clinical observations are reported in detail. Few complaints of the odour of the powder or of skin irritation were made and no real evidence of toxic effects was obtained. The main conclusion is that "Malathion is considered safe for the control of human head or body lice, especially since infrequent applications of small amounts of 1% powder are effective." *M. E. Delafield*

ATMOSPHERIC POLLUTION

BOYD, J. T. **Climate, Air Pollution, and Mortality.** *Brit. J. Preventive & Social Med.* 1960, July, v. 14, No. 3, 123–35, 1 fig.

The association between mortality, particularly respiratory mortality and climate and atmospheric pollution in London administrative county and rural districts of East Anglia has been examined in detail. Mortality from bronchitis and pneumonia appears to be most closely associated with temperature of a fortnight earlier. Heart disease among persons aged 45 and over showed a similar trend. Humidity showed the same relationship with mortality as that of temperature but humidity and temperature were highly correlated. Sulphur dioxide appears to be the most important of the indices of atmospheric pollution. Fog has the most serious effect on mortality when it is accompanied by a very low temperature.

W. J. Martin

Occupational Hygiene

The order in this section is:—**General; Occupational Physiology; Occupational Diseases (Dust Diseases, Poisoning, Skin Diseases, Others); Occupational Psychology; Heating, Lighting and Ventilation.**

GENERAL

SCHILLING, R. S. F., COOPER, Jane & RAFFLE, P. A. B. **Industrial Hygiene Laboratory Services. A Survey of the Needs of Industrial Medical Officers in the United Kingdom.** *Brit. Med. J.* 1960, July 16, Suppl., 35–9.

For various reasons the United Kingdom has been slow in setting up industrial hygiene laboratories to measure environmental conditions and their effects on workers. Although many industrial medical officers are convinced of the need for such laboratories there is little factual information available on the potential demand from industry for such facilities. This paper describes the results of an enquiry made for a sub-committee of the Industrial Health Advisory Committee of the Ministry of Labour into the needs of members of the Association of Industrial Medical Officers. The Association had 590 ordinary members and 358 associates when the enquiry was made. The ordinary members are mostly medical officers employed full-time in industry, and the associates are mostly general practitioners in the National Health Service doing part-time work in industry. The Medical Officers were asked to fill in a questionary dealing with the needs they had experienced over the past two years for tests in connexion with three of their duties: (1) routine surveillance of groups of workers exposed to known occupational hazards (biological tests); (2) routine measurement of the working environment in known occupational hazards; and (2) investigation of suspected occupational hazards. The questionary was sent to 239 ordinary members and 332 associates. Only one questionary from each organization was analysed.

212 (89%) of the ordinary and 237 (71%) of the associate members replied. After omitting those who had not been employed in industry throughout the two-year period of enquiry, there were 378 replies left for analysis, 175 from full-time and 203 from part-time industrial medical officers. For each of the three types of tests, the needs of the full-time medical officers were greater than those of the part-time doctors. 232 medical officers wanted help from a laboratory to undertake biological tests of workers; 29 (13%) of these could not get the help they needed. 225 medical officers said they needed help with routine investigations of the working environment; 70 (31%) of them could not get at least one environment test done. In the investigation of possible hazards, 173 medical officers needed help: 38 (22%) of them could not get help for at least one problem. The majority of the medical officers wanting help said they would have used an industrial hygiene laboratory if one had been available. The enquiry also indicated that the total number of persons in factories with industrial medical officers for whom biological tests are required is measured in tens of thousands and not just a few hundred.

This survey takes no account of the needs of the many thousand factories without industrial medical services. If these services were expanded, the demands for laboratory tests would almost certainly increase. Nevertheless, the results of this carefully planned and executed enquiry indicate quite definitely that steps should be taken to initiate a national industrial hygiene laboratory service.

[Three problems to be faced in developing such a service are: (1) finance; (2) the form of administrative structure bearing in mind the importance of its being an impartial body; (3) the lack of suitably trained personnel.]

P. J. R. Challen

RAFFLE, P. A. B. **Stress as a Factor in Disease.** *Lancet.* 1959, Nov. 14, 839–43, 3 figs. [14 refs.]

Data relating to mortality from coronary artery heart-disease among London Transport employees and other occupational groups of men are considered with particular attention being paid to studies reported by MORRIS and his colleagues [*e.g.*, *Lancet*, 1953, v. ii, 1053 and 1111; *ibid.*, 1956, v. ii, 569; this *Bulletin*, 1959, v. 34, 338] during the last 8 years. One of their earliest and most important findings was that coronary heart-disease, indicated by the first clinical episode, was less common, occurred at a later average age and was generally less severe among male bus conductors than among drivers [*ibid.*, 1955, v. 30, 138]. They suggested three possible reasons for this finding and later studies concerned with these possibilities are briefly described. It is suggested that the evidence so far accumulated indicates (1) "that physical activity of work, by some mechanism not yet understood, protects middle-aged men to some extent from coronary heart-disease", (2) that the difference in coronary heart-disease rates between drivers and conductors is related to differences in constitution between the groups but in a way not yet fully understood and (3) that "there is no epidemiological evidence yet that stress is a factor in coronary heart-disease".

In this context "stress" is defined as "external psychological stimuli due to occupation tending to produce disturbance in the organism" and the possibility of stress playing a part in the production of disease is examined further by reference to sickness absence statistics relating to 4 occupational groups of London Transport employees. The groups considered are (1) Central bus drivers, (2) Central bus conductors, (3) workshop staff at the Chiswick overhaul works and (4) motormen and guards on the Underground Railway. The major difference, apart from the actual work done, between these groups is that the workshop staff, unlike the others, do not work on rotating shifts. Raffle points out that the workshop staff were doing similar work to that done by many light

engineering workers all over the country—"work which could hardly be called 'stressful'."

The sickness absence rates are shown in diagrammatic form by age and occupational group for 1949–52 (1950–52 for motormen and guards). The rates plotted are average annual inception rates of spells of sickness of 4 or more days' duration. Diagrams show the rates for (1) all causes of absence (including accidents) combined, (2) functional nervous disorders (the psychoses and psychoneuroses) and (3) diseases of the stomach and duodenum.

In each age-group male conductors had the highest rates from all causes, and motormen and guards the lowest. The differences between occupational groups were small at ages 30–45 but increased as age advanced. When similar rates were examined for some 20 broad diagnostic groups of cause of absence, the conductors generally had higher rates than drivers of the same age in every diagnostic group.

The author recalls that NORMAN [this *Bulletin*, 1959, v. 34, 132] examined reasons for differences between drivers, conductors and workshop staff in their experience of functional nervous disorders and stomach diseases and his arguments are re-stated. The rates for functional nervous disorders were very similar for all 4 occupational groups, although at all ages motormen and guards had the lowest rates and at 50–60 years the rate for conductors rose to more than twice its level at earlier ages. It is argued that this peak rate is unlikely to be due to stress alone because other age-groups are unaffected. The rates for diseases of the stomach and duodenum rose steadily with age in all occupational groups. At ages 35–45 years the rates for all 4 groups were similar but at younger and older ages, although conductors and drivers had similar rates, these were higher than those of other workers. Again it is concluded that stress alone is unlikely to give rise to these differences.

Raffle suggests that there are two reasons why none of these data support the clinical impression of stress as a factor in physical illness. The first is essentially the inability of the physician to measure "stress" directly so that it can be related to disease incidence. The second is the effect of selection on the composition of occupational groups. Such selection can operate either as self selection by the employee when he avoids or leaves jobs which to him are stressful, or by the employer when he selects men for jobs on the knowledge that they can stand up to the stress imposed by the job. *E. A. Cheeseman*

SOLOVIEVA, V. P. & GAMBASHIDZE, G. M. **[Physiological Basis for a Regime of Work and Rest for Regular Night Shift Workers]** *Gigiena Truda i Professional'nye Zabolevaniya.* Moscow. 1960, No. 7, 17–23, 4 figs. [10 refs.]

The object of this work was the study of the adaption of diurnal physiological rhythms in night shift workers, to establish a basis for planning a regime of work and rest so as to maintain a high level of efficiency. Night workers on the Moscow underground railway were studied. They were mainly aged 30–45 years, with length of service from 6–22 years, and they were working from midnight to 7 a.m., having one rest day a week and 18 working days' holiday a year. Investigations included recording of body temperature, pulse rate, blood pressure, indices of higher nervous activity and "strength", at the same time living conditions were enquired into and sickness absence was studied.

The overall sickness absence of the night shift workers only slightly exceeded that of the day shift workers but for some conditions, *e.g.*, nervous disease, ulcer trouble, bronchitis, etc., the morbidity was doubled. In 20 workers studied over the whole 24 hours, it was found that the diurnal changes in body temperature, pulse, and blood pressure were the same as those seen in persons living on the ordinary regime. As the nature of the work did not allow efficiency to be measured by the usual methods, such as output and quality control, an indirect method of test tasks was employed. This revealed an increase in time for completion of these tasks and in the percentage of errors at 3 a.m. and again at 6 a.m.

It was surmised that the absence of readjustment of diurnal rhythms, despite many years on night work, was caused, to a considerable extent, by unfavourable conditions of rest in day time. This was confirmed by a questionnaire into living conditions, which revealed that 67·3% of workers, particularly the women, had slept only 4½–6 hours after the night shift.

An experimental regime was instituted in which the 13 workers served as subjects. They came straight from work, took a warm shower, changed, breakfasted, and slept in a darkened, quiet room until 12.30 p.m.–1 p.m. At 2 p.m. they had lunch, took a walk in the fresh air and at 4 p.m. they rested again. Supper was at 7 p.m., after which they went to sleep again until 11 p.m. It was found that in nearly all the subjects there was an improvement in practically all the indices used over the night period. But the body temperature, by the 6th day, remained approximately constant. *W. R. Lee*

PETERS, T. Die Druckluftarbeiten beim Bau des Rheintunnels in Düsseldorf. **[Work in Compressed Air during the Building of a Rhine Tunnel in Düsseldorf]** *Zent. f. Arbeitsmed. u. Arbeitsschutz.* 1960, July, v. 10, No. 7, 158–61, 6 figs.

In this paper there is a technical description with photographs of the building of a tunnel under the Rhine which was completed in August 1959 after 6 months of work. The total length of the structure is 904 metres of which 604 metres is the length of the underwater section of the tunnel of diameter 3·45 metres. There is an account of the methods adopted to maintain the health of the workers by a supervising medical officer. A description is given of the treatment adopted for catarrhal conditions which are the chief cause of unsuitability for work under pressure and of the treatment used for incidents of caisson disease. There is mention also of a hot, sweetened herbal tea containing *Herba hyperici*, maté and hops, which was available for all the workers and is stated to have had a welcomed stimulating effect.

In the course of the tunnelling, 713 persons, of whom

313 were men who had presented themselves for employment, were examined. Of the latter, 18 (5·8%) were found to be unsuitable for the work.

96 incidents of caisson disease occurred and the main symptoms in these patients are stated. All cases of the disease were slight and full recovery of all patients ensued. This good experience is attributed not only to the good medical care, the relatively low positive pressure needed at work and the low atmospheric temperature and humidity, but in all probability to the scheme of interrupted work shifts. This scheme is described with a diagram. Each shift was 9 hours and 45 minutes in length. Wages were paid for the whole period during which, however, the total time worked was only 2 stretches of 3 hours separated by a pause for rest, washing and taking food. *M. E. Delafield*

OCCUPATIONAL PHYSIOLOGY

British J. Dis. Chest. 1960, Apr., v. 54, No. 2, 105–99, illustrated. [Numerous refs.] **A Symposium on Disordered Pulmonary Function held at the Queen Elizabeth Hospital, Birmingham on October 23rd and 24th 1959.**

This symposium commences with a survey of the problem of assessment of respiratory function by W. Melville Arnott (pp. 106–112) under the headings of ventilation, diffusion and perfusion, and the interrelation of clinical observations, functional measurements and radiological studies. The development of the dynamic study of ventilation is traced from the static measurement of lung volumes, followed later by the remaining functional zones of diffusion and perfusion.

J. M. Bishop (*Pulmonary Ventilation*, pp. 113–117) surveys the methods of measurement and the causes and effects of various disturbances in this function. Lung volumes are readily obtained from a spirometer, except for residual volume which entails the use of an inert gas. This is rebreathed in a closed circuit until equilibration is complete, after which the fall in concentration in the inert gas gives, by easy calculation, the volume added to the closed circuit from the lungs. The ratio of residual volume to total lung capacity (TLC) is increased in emphysema, old age or where TLC is reduced.

The minute ventilation (respiration per minute × tidal volume) is important especially at standard exercise; it may be obtained by Douglas bag. Alveolar ventilation is calculated by subtracting dead space from tidal volume before multiplying by frequency of respiration. Dead space may be assumed or may be obtained from the Bohr equation.

If carbon dioxide elimination remains constant the ventilation and CO_2 tension of the alveoli ($paCO_2$) are inversely related. Measurement of arterial pCO_2 ($paCO_2$) by puncture or by the rebreathing method described below is of great importance for it may be equated to $paCO_2$, and abnormally high values indicate inadequacy of alveolar ventilation. Abnormally low paO_2 also indicates poor alveolar ventilation but its determination is technically difficult. Owing to the shape of the oxygen-dissociation curve, the more easily determined percentage oxygen saturation of the blood only falls below normal when paO_2 is profoundly depressed and is therefore of limited value.

Low $paCO_2$ indicates hyperventilation which may result from the need for a higher paO_2 in patients with alveolar-capillary block. In these paO_2 will only be maintained in normal range by an increased driving gradient obtained in this way. Exercise upsets the precarious balance, however, and blood oxygen unsaturation may occur.

A further cause of defective alveolar ventilation is mal-distribution or inequality of ventilation. Methods of measuring this are described below.

J. Butler (pp. 118–128) examines the *Mechanical Properties of the Lung*, first by relaxation pressure-volume curve which gives the elastic properties of chest wall and lungs. The pressure-volume curves obtained by the cabinet type of respirator provide a measure of total resistance to flow made up of the airway and tissue viscous resistance of chest wall and lung tissues.

In order to isolate and measure resistance of the lung alone the intrapleural or, more commonly, the oesophageal pressure (which is of the same order) has to be obtained. The slope of the elastic pressure-volume curve, obtained by joining end-inspiratory and end-expiratory points, is the lung compliance (litres per cm. water pressure). The area within the loop, as before, is airway and tissue viscous resistance.

Lung compliance is reduced—the lungs are stiffer—in heart failure, acute pulmonary congestion, pulmonary infiltrations and fibrosis, effusions, deformity and obstructive airway disease.

Lung tissue and airway resistance is greater in asthma, emphysema and bronchitis.

Airway resistance may also be assessed by the record of volume against time during maximum expiration into a spirometer with a fast drum.

The following chapter deals with *The Evaluation of Abnormalities of the Blood Gases*, by P. Harris (pp. 129–132). This section is concerned entirely with the gases in arterial blood. It first describes its normal composition and the dependence of blood *p*H on equilibrium between carbonic acid and bicarbonate.

When dealing with abnormal states there is some overlap with the earlier section on ventilation but a new concept arises, that of ventilation-perfusion ratios. Air must contact blood and good ventilation will fail in its purpose if not balanced by perfusion. The normal ratio is 4 litres air to 5 litres of blood.

J. M. Bishop deals with the *Establishment of a Laboratory for the Assessment of Pulmonary Function* (pp. 133–136). After describing the desiderata for greatest efficiency in tests of lung function, the author

suggests the following methods as minimum requirement: (1) spirometer (Bernstein type); (2) peak flow meter; (3) Douglas bag, dry gas meter and Scholander gas analysis apparatus; (4) Van Slyke apparatus for arterial blood analysis or equipment for Astrup method.

E. J. M. CAMPBELL and J. B. L. HOWELL, (*The Rebreathing Method of Estimating Arterial and Mixed Venous CO_2 Tension*, pp. 137–138) noticed that the rebreathing of any CO_2 mixture from 0 to 100 mm.Hg for 1–1½ min. produced a P_{CO_2} of such an order that subsequent rebreathing (for 20 seconds or 5 breaths, whichever is longer) from the same bag, after 2 minutes' interval, produced a mixture of the same P_{O_2} as mixed venous blood. The subtraction of 6 mm.Hg yields arterial P_{CO_2}.

A. G. W. WHITFIELD writes on *Functional Aspects of Pulmonary Disease. The disordered physiology of obstructive bronchial disease*, (pp. 139–145). The lower limit of normal for the 1-second timed-vital-capacity (TVC) is certainly less than the 80% given here. This is nevertheless an excellent account of the genesis of emphysema from bronchiolar narrowing in bronchitis and asthma. The ventilatory insufficiency manifests itself as marked slowing of expiration, giving reduced maximum expiratory flow rate and TVC measurements. The tidal excursion is situated nearer the maximum expiratory position than is normal—the residual volume is increased, both absolutely and relatively. The account of progress of the disease to alveolo-respiratory insufficiency and cor pulmonale should be read in the original work.

W. MELVILLE ARNOTT writes on *Alveolar-Capillary Block* (pp. 146–156). In alveolar-capillary (A-C) block there is commonly increased "dead space" (due to extensive obliteration of the pulmonary capillary bed), pulmonary hypertension and perhaps right heart failure. It should also be remembered that conditions which cause A-C block are also likely to alter ventilation-perfusion ratio. The limitation is also stressed that diffusing capacity (D_{CO}) is a feature of the whole membrane and not of unit area. [K_{CO}, which is mean permeability per unit volume, approximates more closely to a specific membrane index.] The various methods for measuring D_{CO} are critically evaluated. Pathological, clinical and radiological features are also described and the chapter closes with sections on diagnosis and treatment.

In the 2½ pages of his article (*The Management of Respiratory Infection*, pp. 157–159) A. B. TAYLOR sketches the commonly encountered types of respiratory infection. Common cold, influenza and adenoviruses are prone to excite secondary bacterial infection. The value is discussed of antibiotics, cortisone, trypsin inhalers, vaccines, oxygen and antispasmodics. Tracheotomy is of great value in respiratory obstruction with CO_2 retention and right heart failure. It should be remembered that fungal infections may be superadded and that tuberculosis appears to be on the increase in the elderly, particularly males.

The last 100 cases admitted under the author's care are reviewed here (*The Management of Status Asthmaticus*, by D. R. HUMPHREYS, pp. 160–167). Those of infective origin outnumbered the allergic, which in turn were more numerous than the psychological.

Adrenaline and ephedrine are effective in most cases of asthma; indeed status asthmaticus is mainly the result of adrenaline fastness. Aminophylline and corticosteroids are used when adrenaline produces no effect. The routes for administration and dosage of these newer drugs and their derivatives are discussed in considerable detail.

This section includes paragraphs on complications, on sedation and on other forms of treatment, *e.g.* inhalation of detergents, bronchoscopy and oxygen-helium mixtures, all of which have a limited usefulness in treatment of certain patients.

J. BUTLER (*Assisted Respiration in Respiratory Disease*, pp. 168–174), gives 3 main indications for assisted respiration: (1) depression of respiratory centre, (2) post-operative carbon dioxide narcosis, and (3) chronic bronchitis, asthma, emphysema and the hypoventilation syndrome. Carbon dioxide elimination is assured by this method and oxygen can be given in adequate concentration.

The relative merits are discussed of cabinet respirators and intermittent positive-pressure ventilation through a tracheotomy tube which is considered the method of choice.

There is much helpful detail about bronchial aspiration, humidification, monitoring of tidal volume (which should be carried out on expired air) and general management.

Here again is an up-to-date account of the lung vascular mechanics which are only now being elucidated (*The Lungs and Heart Disease—Pulmonary Haemodynamics*, by K. W. DONALD, pp. 175–181). The author sketches the pressure-flow relationships, anatomy, central and peripheral control of flow, and relation to diffusing capacity of the pulmonary circulation.

The reservoir action of the lung circulation is attributed to the pulmonary veins which alone are sufficiently distensible. The author admits that pulmonary instantaneous capillary content increases from 80 to 170 ml. but claims nevertheless that most of the 4- or 5-fold increase in diffusing capacity caused by exercise is due to reduction in intra-capillary impedance rather than to increased surface area of the blood gas interface.

Progressive histological changes develop in media and intima of muscular pulmonary arteries and arterioles in the presence of chronic pulmonary hypertension from congenital septal dejects. These are described (*Pathology of the Pulmonary Vessels*, by D. HEATH, pp. 182–185) under 6 grades: the first 4 are proliferative, the remainder are dilatation lesions which may be distended arterioles or plexiform, angiomatoid or cavernous in nature.

In grades 1–3 resistance in the vascular bed, although high, is labile; in grades 5 and 6 resistance is no longer labile. Grade 4 is transitional.

P. DAVISON writes on the *Functional Aspects of the Cor Pulmonale Syndrome* (pp. 186–190). Cor pulmonale may arise from arterial hypoxia or from increased intrapulmonary resistance. Hypoxia may be due to alveolar hypoventilation (as in emphysema), alveolar-capillary block or intrapulmonary or intracardiac shunts and produces its cardiac effects by changing systemic vasomotor tone or by increasing blood volume, erythrocyte content, haematocrit and consequently blood viscosity.

Increased resistance to lung blood flow may arise from reduction in capillary bed, diffuse parenchymatous

disease, thrombo-embolism, external pressure or as a life-long concomitant of congenital cardiac defect. Congestive cardiac failure may also be causative and in a few cases the initiating factor is still unknown. The end result is respiratory or right ventricular failure.

The remainder of this section is devoted to more detailed discussions of cor pulmonale heart failure, emphysema cor pulmonale, thrombo-embolic cor pulmonale and primary pulmonary vascular disease.

L. A. G. Davidson and A. L. D'Abreu (*Effects of Surgery on Pulmonary Function*, pp. 191–199) warn that operations for excision of lung are frequently carried out with too little knowledge of lung function.

After pneumonectomy lung function is generally much better than 50%, *e.g.* the maximum breathing capacity is often 80% of the preoperative values. In ankylosing spondylitis resection of lung is usually well tolerated compared with upper abdominal operations which interfere with abdominal respiration.

Massive lobar atelectasis was found in 35% of 88 patients after abdominal surgery and smaller lesions in a further 20% ; the extent correlated well with reduction of 1-second forced-expiratory-volume (or 1-second TVC) and with the degree of pneumoperitoneum.

Other changes reported after abdominal operation in this very interesting account are, a fall in all compartments of lung volume, expiratory flow rate and arterial oxygen saturation. *M. L. Thomson*

OCCUPATIONAL DISEASES

Hasselt: Institut D'Hygiène Des Mines. Communication hors-série. Les mesures d'empoussiérage dans les charbonnages belges [Degueldre, G.]. [**Dust Measurements in Belgian Coal Mines**] [Reprinted from *Geologie en Mijnbouw*. (n.s.) 1959, Sept., v. 21, 300–19, 16 figs. (34 refs.).]

This is an elementary and uncritical description of methods of measuring dust for routine purposes and for research The following are dealt with: hand-pump and densitometer, with details of the official procedure adopted by the Mines Administration ; British konimeter; Soxhlet thimble gravimetric method; thermal precipitation ; membrane filter. A short account is given of the determination of silica by chemical and physical methods. *C. N. Davies*

Houberechts, A. Problèmes actuels de la ventilation des mines. [**Current Problems in Mine Ventilation**] Reprinted from *Publications Ass. Ingénieurs Facul. Polytechnique de Mons.* 1959, Fasc. 1, 12 pp., 5 figs. [61 refs.]

Mine ventilation was originally conceived in terms of the supply of oxygen necessary for respiration with a passing concern for firedamp concentration, the figures recommended being 30 litres per second per head in workings free from firedamp and 60 litres per second elsewhere. Later, the idea of security dominated the problem and ventilation rate was defined, without reference to the number of persons at work, to keep the concentration of methane in the return air between 0·5 and 1%. Recently the dilution of gases from shot-firing and diesel haulage has had to be considered, the latter demanding 100 l/sec. per kW of power between limits of 2 and 10 $m.^3$/sec. To this is added dust control, for which a delicate balance has to be struck between dilution and re-dispersion. The idea of hygiene is thus added to that of safety. Now, in the deepest mines, where the rock temperature is around 45°C., the highest possible rates of ventilation are demanded unequivocally in order to maintain a tolerable climate for the miner. This problem is examined in detail in the paper.

The amount of work a man can perform is related to the difference between the heat he develops by metabolism plus the heat received from his surroundings by radiation and convection, and the heat which he is able to liberate. The method of calculating this heat balance, in terms of wet- and dry-bulb temperatures and air velocity, is outlined. In order to obtain a significant output of labour it is necessary that the workman should be able to dissipate about 250 kcal. per hour ; other things being equal, increasing the ambient air speed relieves the worker of heat stress but, at the same time, enhances his sensitivity to wet-bulb temperature.

Increasing the amount of air which passes down a roadway cut through warm rock also helps to keep the dry-bulb temperature down. Calculations, for a specific example, are given which show the increase in temperature along a dry roadway for distances up to 2,600 m. and air flows between 37·5 and 150 kgm. per second. If the surface is wet a similar improvement with air mass circulated is obtained, but the gain declines as the ventilation rate increases. High air turnover is important even when refrigeration is in use.

An examination of the relationship of the depth of the mine to the heat which has to be removed leads to the conclusion that when the depth increases from 600 to 1,200 metres the heat to be dissipated by ventilation rises from 20,000 to 75,000 kcal. per metric ton net of coal won. This is on the basis of 5,000 kcal. being contributed by machinery and human metabolism, the rest coming from the strata and from the oxidation of coal ; these heat figures are considered minimal.

Ventilation can be increased by raising the fan power and by reducing the aerodynamic resistance of the airways. The shafts offer a large part of the total airway resistance, sometimes as much as 50%, but this can be reduced by using frontal guiding with a large section separated from a smaller one in which pipes and ladders are disposed. The resistance coefficients of shaft walls

and longitudinal and transverse obstacles are discussed and, in the case of the latter, values for the resistance coefficients of variously shaped struts show that a streamlined one has only a quarter the resistance of a square one.

An account is given of three ways of computing the relative strengths of the ventilation currents flowing through the system of airways below ground; these are graphical, by successive numerical approximation and by electrical analogue.

In conclusion it is stated that the majority of Belgian mines pose no climatic problems but that their deepening and the extension of ventilation circuits may result in a progressive deterioration of the working environment which can only be prevented by improved ventilation; the basic factors are airway resistance and the distribution of flow through the various channels.

C. N. Davies

KING, E. J. & FLETCHER, C. M. [Edited by.] **Industrial Pulmonary Diseases.** A Symposium held at The Postgraduate Medical School of London, 18th-20th September, 1957 and 25th–27th March, 1958. pp. viii + 273, 98 illustrations. 1960. London: J. & A. Churchill Ltd., 104, Gloucester Place, W.1. [32s.]

The 21 papers read at the Symposium cover the story of dust inhalation and its effects, beginning with the passage of dust particles from the external air to the alveoli.

C. N. DAVIES in *Deposition of Dust in the Lungs* (pp. 44–58) shows that the laws of physics decide the amount and size range of particles reaching the alveoli. Only one-third of the dust deposited in the alveoli is retained, the rest is removed by phagocytes *via* the air passages. The retained third is transported into the lung either by phagocytes or as free particles. The action of the dust then depends on its nature, a subject dealt with by E. J. KING and C. V. HARRISON in *Reaction of the Lung to Dust* (pp. 37–43). By injecting dust of respirable size intratracheally into animals it was found that coal dust does not excite fibrosis while silica has a characteristic fibrogenic action. A mixture of the two produces more fibrosis than the sum of the two alone. Coal dust injected along with an avirulent strain of tubercle bacillus gives a reaction out of all proportion to the effects of the two alone.

The origin of the characteristic silicotic fibrosis is discussed by G. NAGELSCHMIDT in *A Review of the Theories of Silicosis* (pp. 59–68). He gives an account of the loss of favour of the silica solubility theory and of the substitutes that have been suggested. The effects of dust in the lung are described by J. GOUGH and A. G. HEPPLESTON in *The Pathology of the Pneumoconioses* (pp. 23–36). They compare the simple pneumoconiosis of coal workers with simple silicosis. Serial sections of coal-miners' lungs show that a sleeve of dust and a minimal fibrosis is formed round the respiratory bronchioles and these bronchioles dilate to produce focal emphysema. Reasons are given for believing that tuberculosis is the complicating factor in producing massive fibrosis. Asbestosis presents a different type of fibrosis arising from a chemical or mechanical cause. The mechanical hypothesis is in favour at present.

Three papers are devoted to the use of radiology in diagnosis. Two of these, *Problems in Taking and Reading Chest Radiographs*, by G. SIMON (pp. 69–71), and *Radiography in the Field*, by P. J. CHAPMAN (pp. 78–93), are concerned with the technique for radiography required for this work. These papers should be studied by all radiologists responsible for making films of chests of patients exposed to dust. The difficulty of obtaining satisfactory films is apt to be underestimated. The third paper on the subject, *Radiological Diagnosis of Pneumoconiosis*, by C. M. FLETCHER (pp. 72–77), mentions among other things the classification of X-ray abnormalities laid down by the ILO Conference on Pneumoconiosis at Sydney in 1950 [this *Bulletin*, 1954, v. 29, 626]. This is a modification of a classification made for coal workers by the Pneumoconiosis Research Unit. It is most suitable for coal-miners, but less so for those who work with silica where the nodules may be limited to the upper parts of the lung. It is not suitable at all for cases of asbestosis and aluminosis. A later classification produced at Geneva in 1959 [*ibid.*, 1960, v. 35, 21] lays the emphasis on the size of the nodule rather than distribution.

Disablement in pneumoconiosis largely arises from dyspnoea, and physiological tests are used to measure this. P. HUGH-JONES in *Normal Lung Function and its Measurements* (pp. 94–109) gives a list of tests for clinical use. A warning is given against equating single tests with testing lung function. In many pneumoconiotics, however, a defect in ventilatory capacity is the major change, so that this test may provide a good assessment. In asbestosis the defect is in the diffusing capacity of the alveolar interface: this has been confirmed since the publication of this book, by WILLIAMS and HUGH-JONES (p. 1175). J. C. GILSON in *The Disturbance of Pulmonary Function in Industrial Pulmonary Disease* (pp. 110–126) shows that simple pneumoconiosis causes little disturbance in the young and middle-aged, when the dust is biologically inert; fibrogenic dusts lead to a reduction in the maximum breathing capacity (MBC). Complicated disease produces reduction in ventilatory capacity and gross inequality of gas distribution. Cotton cardroom workers were found to have a fall in forced expiratory volume during the day's work, while coal-miners did not. This acute effect in cotton workers may be a help in reaching a safe level for dust in that industry. Tests for use in the field must be simple, accurate and independent of the patients' co-operation according to C. B. MCKERROW in *The Use of Pulmonary Function Tests in Epidemiological Work* (pp. 127–138). The apparatus for measuring forced expiratory volume, and Wright's Peak Flowmeter [*ibid.*, 1960, v. 35, 850], are described.

Various surveys of populations are described in two papers. A. L. COCHRANE in *Epidemiology of Coalworkers' Pneumoconiosis* (pp. 221–231) observed that the mortality rates and the physiological results found in the Rhondda Fach survey were different in miners with no pneumoconiosis from those in miners with simple pneumoconiosis; possible causes for this difference are given. Five theories are put forward to explain massive fibrosis: the tuberculosis hypothesis has a little more support than

the others. The other paper, *An Approach to the Problem of Bronchitis in Industry: Studies in Agriculture, Mining and Foundry Communities*, by I. T. T. HIGGINS (pp. 195–207) describes surveys in the Rhondda, Leigh and Staveley where miners and ex-miners had more "chronic bronchitis" than men who had never worked in the mines; they had also a lower MBC. No striking excess of bronchitis was found in the foundry workers of Staveley.

Two papers are concerned with radio-opaque dusts, and benign pneumoconiosis. In these cases there is no fibrosis, no massing and no disability. In *Pneumoconiosis due to Tin Oxide*, A. J. ROBERTSON (pp. 168–184) gives a description of tin smelting and the effects of dust. Tin has an atomic weight of 118, and gives rise to an extremely dense nodulation. A. I. G. MCLAUGHLIN in *Iron and other Radio-opaque Dusts* (pp. 146–167) says the benign condition occurs in electric-arc welders, silver finishers, and ochre-miners and millers. In electric-arc welding irritating gases may cause emphysema. Foundry workers, boiler scalers and emery workers may have mixed-dust fibrosis since silica dust may be inhaled along with the iron.

L. W. HALE in his paper on *Pneumoconiosis in Cornwall* (pp. 139–145) deals with the classical silicosis of tin-miners and granite dressers. In the china-clay industry there is a risk of a pneumoconiosis of the coal-miners' type in those who work in the processing and bagging. The massive lesions, however, are of a whitish-grey colour contrasting with the black colour of the coal-miners' fibrosis. In parenthesis it may be remarked that the china-clay lesion has been observed outside Cornwall, in leather dressers who use china clay.

A. CAPLAN tells us in *Rheumatoid Disease and Pneumoconiosis* (pp. 232–240) of the syndrome which goes by his name. It has been found in workers exposed to dust of many varieties. Sometimes it occurs without any sign of arthritis but then a familial incidence of rheumatoid arthritis may be found. Corticosteroid treatment produces no change in the lesions in the lung. The question of the relationship between cancer of the lung and the pneumoconioses constantly turns up. It is dealt with by R. DOLL in *Occupational Lung Cancer* (pp. 208–220). No evidence is found to incriminate iron, coal or silica; but asbestos is placed as an established risk.

Byssinosis is legally not a pneumoconiosis in the United Kingdom, since it is not a fibrosis of the lung. R. S. F. SCHILLING explains, in *The Epidemiology of Byssinosis* (pp. 185–194), that in the early stages it is easily distinguished from bronchitis by the history of the attack; later the distinction is not so clear. It is not an allergic reaction as in asthma for the effect of the dust is gradual and is not reversed by anti-histamine drugs.

J. Donald BALL sums up the position in regard to complicated pneumoconiosis, in *The Natural History and Management of Coalworkers' Pneumoconiosis* (pp. 241–254) by saying that one can do much to alleviate the symptoms and enable the patient to accept his disability, by a thorough assessment of physical, emotional and social aspects of the disease and by meticulous treatment of bronchitis and tuberculosis complications.

A. MEIKLEJOHN in *Industrial Pulmonary Diseases in Great Britain* (pp. 1–22) says that no one knows the prevalence of dust diseases of the lungs in Great Britain; but a rough estimate can be made from statistics published in the annual *Report of the Ministry of Pensions and National Insurance* (HMSO), and for coal-miners in the *Digest of Pneumoconiosis Statistics* published annually by the Ministry of Power. He says that 2 points require investigation, namely the continued production of cases in young coal-miners in the South Western division, and the low incidence of diagnosed cases in the East Midlands Region. D. HUNTER completes the symposium by his paper on *The Prevention of Silicosis* (pp. 255–269) when he gives details of the substitution of safe for dangerous materials, of the methods of suppression of dust, of personal protection of the workers and of other means of lessening the risk.

Like all books consisting of papers by a number of writers, this one contains some overlapping. The subject is, however, well covered and the volume is one which should have its place—a prominent one—in the library of everyone who has to do with pneumoconiosis.

Charles L. Sutherland

EDMONDS, O. P. & KERR, D. S. **Observations on the Occupational Life History of the Coal-Face Worker at Two Collieries.** *Brit. J. Indust. Med.* 1960, July, v. 17, No. 3, 234–7, 2 figs.

The life-history of coal-face workers was studied at 2 collieries in the East Midlands Division (Nottinghamshire and Derbyshire) of the National Coal Board, Great Britain. At colliery A 1,725 men, of whom 706 were coal-face workers, were employed; the corresponding figures for colliery B were 1,637 and 806. Environmental conditions at colliery B were more severe than at colliery A; the coal seams were thinner, there was less mechanical loading and temperatures, dry and wet bulb, were higher. During 1957 and 1958 at colliery A 36 workmen were downgraded from the coal-face and in 1957 37 at colliery B [no explanation is given of this variation in the years]. These 73 workmen constitute the population studied.

Analysis by age-group showed that face-workers left the coal-face at all ages but the highest incidence was after the age of 44 years—under 45, 17·8 per 1,000 per annum, over 44, 62·1 per 1,000 per annum. The main factors which determined leaving the coal-face were injury (41·0%), illness (34·2%), death (8·1%) and general fatigue and voluntarily (16·4%). The same overall pattern was noted at both collieries but, as might have been anticipated from the differences in general working conditions, the wastage at colliery B exceeded that at colliery A. While some endured coal-face work for only a few years, the fittest completed 33·3 years; the mean was 21·3 years. Face workers, particularly the older more experienced men, for various reasons including status and prestige, preferred to transfer to other work underground rather than to work on the surface. Accordingly, cumulatively over the years, a large proportion of underground workers were ex-face workers. It has frequently been recorded that the mortality for coal-face workers is less than that of coal-miners employed elsewhere [this *Bulletin*, 1958, v. 33, 1143]. This simply proves that self-selection is

at work whereby only the fittest can maintain face work. The authors suggest that important information about the health hazards of face workers might be gained by a study of other underground workers. *A. Meiklejohn*

GRAILLES, M. Intérêt de la méthode des coupes totales de Gough et Wentworth pour l'étude anatomo-pathologique du poumon pneumoconiotique. [**Application of the Large-Section Technique of Gough and Wentworth to the Study of Pulmonary Patholcgy in Pneumoconiosis**] *Rev. Méd. Minière.* Sin-le-Noble. 1960, v. 13, No. 41, 3–14, 16 figs.

This appraisal of the large section technique of GOUGH and WENTWORTH gives a very favourable opinion of the method for the study of pulmonary pathology. It was applied to lungs of coal miners in the Pas-de-Calais. There are several whole page illustrations which show that the method was successfully used although the reproductions are not all perfect. The sections were found of particular value in distinguishing the various types of pneumoconiotic change. The technique is regarded as essential for the assessment of emphysema, although the distinction between centrilobular emphysema due to bronchiolitis and focal emphysema due to dust requires histological study. The findings in general show very clearly that the lesions in coal-miners in France are very similar to those in Wales. *J. Gough*

LONGLEY, M. Y. **Pulmonary Deposition of Dust as affected by Electric Charges on the Body.** *Amer. Indust. Hyg. Ass. J.* 1960, June, v. 21, No. 3, 187–94, 3 figs. [25 refs.]

Mice, restrained in glass tubes, were exposed to aerosols of potassium chromate containing particles smaller than 5 microns with 80% below 0·5 micron. 3 groups of animals were employed, 1 at earth potential, 1 charged positively and the other negatively; the charged animals were at 4,000 volts. The chromate particles carried charges which were not elucidated in detail.

After exposure the animals were killed and the chromium content of the lungs was determined. In each case more chromium was found in the animals which had been earthed during exposure but there was no significant difference between positively and negatively charged animals.

Since the body of the animal is conducting no electric field due to a charge upon it exists inside. The observations of this experiment are therefore probably associated with the attraction or repulsion of particles as they approach the nose, immediately before inhalation.

C. N. Davies

PARRISH, H. M. & ASHE, H. B. **Epidemiologic Methods in the Study of Silicosis.** *Arch. Environment. Health.* Chicago. 1960, Aug., v. 1, No. 2, 129–39, 1 fig. [52 refs.]

It is proposed to carry out an investigation to determine the efficacy of dust control in preventing silicosis. This will be the first investigation in the United States in which the total population at risk is studied in detail. Methods of epidemiological research in pneumoconiosis previously used in America and elsewhere are considered, and then the various points to be observed in the present study are given. Dust control was initiated in the Vermont granite industry in 1937 but yearly X-ray examinations of workers, and dust counts, were carried out regularly before and since that date.

As the test is of efficacy of dust control, those workers who were employed before 1937, whether still employed or not, need not be considered. The population at risk, that is those who started to work after 1937, whether still employed or not, should be studied in detail. Serious detective work on the part of the epidemiologist will be required to trace those who have left the employment and suggestions are given as to the most fruitful sources of information. Those who have left the employment may yet develop silicosis and should be followed up by annual X-ray examinations. The length of time from entering the industry to a diagnosis of the disease is of practical significance in prevention and control.

A number of workers will for various reasons have missed X-ray examination and a random sample of these should be investigated. The radiological examination in itself provides sufficient information; only those showing suspicious or positive findings need be investigated further. The importance of the International Labour Office Classification of Pneumoconiosis, 1950 and 1959, is stressed, and the questions of observer error and the use of standard films for the diagnosis as advocated by FLETCHER and OLDHAM [this *Bulletin*, 1952, v. 27, 64] are discussed. It is suggested that each film should be read by 3 observers: if there is disagreement there should be a conference. As some minor linear opacities may be the result of early silicosis, a control group of workers from non-dusty trades should be compared, to show what proportion of these are to be expected in normal persons. An accurate industrial history of each worker including occupations in periods away from the industry, is essential.

The data concerning dust counts collected at Vermont are being analysed, and the question of extending their scope is considered. It is emphasized, however, that research methods should remain constant in the long-term studies, for example, light field counts should not be changed to dark field counts. The sampling procedure devised by OLDHAM and ROACH [*ibid.*, 1952, v. 27, 938] is valuable in such studies as the present.

Charles L. Sutherland

VOLK, H. **The Health of Workers in a Plant making Highly Dispersed Silica.** *Arch. Environment. Health.* Chicago. 1960, Aug., v. 1, No. 2, 125–8, 3 figs.

Aerosil is the name given to a highly dispersed, chemically pure silica, produced in the gas phase, by the hydrolytic decomposition of silicon tetrachloride in an oxyhydrogen flame. The water-free product is 99·8% silica. The particles are spherically shaped, of a very uniform size of 5–40 mμ. By X-ray, the oxide is seen to be amorphous. A list of the uses of this product is given.

The workers at the factory in Rheinfelden, Baden, where this silica is produced, have been examined by X-ray every 6 months since 1947 and yearly since 1958. Of the 215 persons examined, 44 were workers of long experience, and 9 were employed over 10 years.

Over the period, the degree of air contamination has been reduced but it is calculated that 120 mgm. are inhaled per day and 25 gm. per year. If this fine silica actually causes silicosis this amount should have produced silicosis in the time. The only signficant observation in the 720 radiographs of the 215 workers was a hair-line accentuation of the interlobar fissures suggesting interlobar pleuritis. It is not possible to state if this pleuritis is caused by silica dust or is a result of a non-specific lung infection. Volk is satisfied however that in the period 1947–59, not a single case was found in which any change was noted which could possibly have been caused by silica as a result of contact with the product. This observation should be linked up with animal experiments carried out by SCHEPERS *et al.* on this dispersed silica [this *Bulletin*, 1958, v. 33, 589, 590, 591].

Charles L. Sutherland

BARRIE, H. J. & GOSSELIN, L. **Massive Pneumoconiosis from a Rock Dust containing No Free Silica. Nepheline Lung.** *Arch. Environment. Health.* Chicago. 1960, Aug., v. 1, No. 2, 109–17, 8 figs.

A fatal case of pneumoconiosis is reported in a man aged 35 who was employed in the mill of a nepheline mine for 4 years. Nepheline rock is crushed to a fine powder for use in manufacturing glazes for pottery. The man worked in the mill where the dry powder was passed over magnetic rollers to remove haematite. Nepheline is a plutonic rock and consists mainly of the felspar albite. The presence in this rock of nepheline syenite is stated to be an indication that during its formation no free silica is present. The rock is hard and is composed of mixed sodium, potassium and aluminium silicates.

The man died 5 years after leaving the nepheline mine, after a gastrectomy operation for duodenal ulcer which left an abdominal fistula, and a second operation of adrenalectomy for Cushing's syndrome. Previous to his operations he had had 3 attacks of bronchopneumonia. The actual cause of death was not determined but there was respiratory failure at the end.

At post-mortem, areas of massive consolidation, white in colour, were found in the lower parts of both lungs. In other parts the histological findings were deposition of dust in the alveoli with no dilation of the respiratory bronchioles—no focal emphysema. In areas of massive consolidation, the alveolar lesions had organized into plugs of cellular tissue which extended up as far as the respiratory bronchiole. In most severely affected areas there was cavitation. No tuberculosis was found.

Lung analysis showed 14·3% total silica, with no free silica. Silicates comprised 54·7% of ash. X-ray diffraction showed that the dust in the lung was composed of felspar albite, under 20% being nepheline syenite. The fibrosis produced may have been due to the physical properties of this albite which forms sharp fibre-like crystals. Nothing resembling asbestos bodies was found. The action of cortisone during the period of evolution of the pneumoconiosis may account for the scantiness of interstitial collagen and the experiments of MARGAREY and GOUGH [this *Bulletin*, 1952, v. 27, 753] are quoted in support of this view.

The massive lesions are attributed to the inert dust producing negligible structural lesions besides lymphatic block. Superadded pulmonary infection prevented resolution of the alveolar exudates, fibrosis occurred and necrosis supervened because of the obliterative endarteritis. Massive fibrosis might well be due, as in the case, to recurrent attacks of bronchopneumonia whether of bacterial or viral origin; this differs from GOUGH'S view that all such masses are due to tuberculosis (*Modern Trends in Pathology, Ed.* COLLINS, D. H., London, 1959, Butterworth & Co. Ltd., p. 273).

Charles L. Sutherland

WILLIAMS, R. & HUGH-JONES, P. **The Radiological Diagnosis of Asbestosis.** *Thorax.* 1960, June, v. 15, No. 2, 103–8, 6 figs.

11 experienced observers comprising 2 panels, examined 53 chest X-ray films, the only information given them being that the films were from normal subjects, and patients with asbestosis and other chronic fibrotic lung diseases. Actually there were 38 from cases of asbestosis—21 certified cases, 7 atypical cases and 10 from patients who had had prolonged exposure to asbestos but who were symptomless and whose X-ray films had previously been regarded as clear. [It is not stated how the diagnosis of asbestosis was made in these 10 cases.] The interpretations of the individual observers were analysed. In general there was good agreement about the normal films, but very wide differences of opinion about the other classes and sub-classes. For instance of the 10 films of patients exposed to asbestos but radiologically reported as clear previously, the number regarded as normal varied from 1 to 8 (stated as 10% to 80%) and as showing asbestosis from 0 to 5 (0% to 50%).

In regard to films considered to be consistent with asbestosis, observers were asked to record the severity of mottling, and the presence or absence of shaggy border to the heart, pleural reaction, and bullae. One panel of 5 observers were provided with 3 standard films selected to represent slight, moderate and marked grades of mottling in asbestosis with which to compare the films being examined. Here again very wide observer variation was noted, of such an extent that in the case of one panel 2 films and in the case of the other 7 films were recorded as showing no mottling, or slight, moderate or marked mottling by different observers. The other radiological signs such as shaggy heart, pleural reaction and bullae were also assessed with wide variation.

The extent of the disagreement of these observers was quite remarkable and the authors conclude that the radiological appearances of asbestosis are by no means specific except in advanced cases and that the use of standard films in diagnosis and grading needs further trial.

A. T. Doig

WILLIAMS, R. & HUGH-JONES, P. **The Significance of Lung Function Changes in Asbestosis.** *Thorax.* 1960, June, v. 15, No. 2, 109–19, 6 figs. [26 refs.]

Clinical radiological and lung function studies were made on 40 patients, grouped as 21 certified cases of asbestosis, *i.e.* with definite clinical and radiological evidence, 10 patients with exposure to asbestos dust for varying periods, but who had no symptoms or signs, and whose radiographs had been classed as clear, and 9 suspected cases. Actually it seems that the second group of 10 patients included some who could have been classed as suspected, for the X-rays of 4 of them were later thought to show varying degrees of mottling and 7 had certain other evidence of asbestosis, *e.g.* finger clubbing or crepitations.

The functional changes in the first group of 21 certified cases were remarkably constant and consisted of a lowered overall diffusing capacity of the lungs; a reduced inspiratory capacity; hyperventilation on exercise, and a lack of evidence of air-flow obstruction unless the disease was complicated, as in two cases, by asthma or emphysema. The severity of the breathlessness was related to the diffusion effect. Individual susceptibility was undoubtedly an important aetiological factor. Other points of interest included changes in the plasma proteins and a large ventilation-perfusion ratio inequality.

The results in the second group suggested that changes in pulmonary function, particularly the lowered diffusing capacity, may precede clinical or radiological signs—an important observation in view of the marked observer variation in the assessment of physical signs and radiographs especially in the early stages of this disease.

The third group was difficult to assess but a fairly firm conclusion as to the presence of asbestosis was arrived at in 6, because they showed the functional pattern of interstitial fibrosis: a reduced diffusing capacity and a relatively well maintained ventilatory capacity. Of 4 in whom exercise oximetry was performed, 3 showed marked desaturation.

This study shows that lung function tests have an important part to play, not only in the assessment of the degree of disability in asbestosis, but in the diagnosis.

A. T. Doig

LEATHART, G. L. **Clinical, Bronchographic, Radiological and Physiological Observations in Ten Cases of Asbestosis.** *Brit. J. Indust. Med.* 1960, July, v. 17, No. 3, 213–25. [Numerous refs.]

10 subjects with asbestosis, 8 men and 2 women, aged 45–65 years were kept under observation for periods of up to 8 years. All were investigated clinically and radiologically, including bronchography of one or both lungs [the films were taken in "antero-posterior" position; the usual position is postero-anterior]. They were also investigated by a battery of physiological tests of pulmonary function. For this part of the study a control group of 11 asbestos workers, boiler laggers, whose chest radiographs were interpreted as normal by 3 independent observers, were used.

The findings are comprehensively set out in 8 tables and an appendix. A detailed account is given of the physiological tests, which included measurement of dynamic compliance and vital capacity, diffusing capacity for carbon monoxide, maximum voluntary ventilation and work of breathing, ventilation equivalent and arterial P_{CO_2} and dead space effect.

In Part 1, clinical and radiological findings, attention is focused on clubbing of the fingers [no reference to toes] and bronchiectasis. 6 cases revealed bronchiectasis bronchographically. The author concludes that clubbing of the fingers and coarse crepitations represent bronchiectasis rather than uncomplicated asbestosis and he suggests that the prevalence of bronchiectasis is higher than has been reported previously, possibly because the patients survived longer than in the 1930s when the cases of asbestosis were more advanced.

[The early writers on asbestosis, 1927 onwards, were not unaware of the high frequency with which some degree of anatomical dilatation of the bronchi was apparent at necropsy. The crux of the matter is the connotation of the term bronchiectasis. This is exemplified by GLOYNE (*Silicosis and Asbestosis,* Ed. A. J. LANZA, 1938, Oxford University Press, p. 228) "the writer has not seen a typical *extensive purulent bronchiectasis* such as is sometimes described in chronic fibroid lung of non-industrial origin". MEIKLEJOHN (*Industrial Medicine and Hygiene,* Ed. E. R. A. MEREWETHER, London, 1956, Butterworths Medical Publications, v. 3, p. 115) similarly recorded that "Despite the frequency of clubbing of the fingers, *frank infective bronchiectasis* is unusual." [Italics not in original.] Again in 1958 Meiklejohn (*Modern Trends in Diagnostic Radiology,* Ed. J. W. MCLAREN, London, 1948, Butterworths Modern Trend Series, p. 64) with reference to the use of bronchography in pneumoconiosis cases wrote, "By reason of the dangers attendant on its use in seriously damaged lungs, this should only be undertaken in cases of extreme diagonistic difficulty. It is seldom required, though on occasion it may reveal areas of unsuspected bronchiectasis". Dr. Leathart himself realized this for "bronchography was restricted to one lung because of severe dyspnoea". It is to be hoped that scientific curiosity will not induce a spate of intensive investigations of pneumoconiosis cases by bronchography.

As to clubbing of the fingers, its prevalence and significance in the diagnosis of abestosis, it may not be inappropriate to record the following hitherto unpublished incidents.

About 25 years ago a colleague and myself were carrying out the prescribed annual periodical medical examinations at an asbestos textile factory. One workman stubbornly refused to be examined and when pressed for a reason said "You doctors are wasting your time tapping and sounding chests. I can tell when a man has caught *it.*" I immediately signified my willingness to learn from him. He led us to the brake-lining department the workers from which were not subject to routine examinations. Many of the men there however, had previously worked for several years in the dangerous processes. We walked round the shop and our professor asked each of his mates in turn to stretch out his fingers so that his pupils might observe the gross drumstick clubbing. This was his diagnostic sign. A year later at the same factory we concentrated on this sign. A man, apparently impressed by the care with which I

studied his typical clubbed fingers, remarked "Doctor, you seem very interested in my fingers, would you like to see my toes? They're the same."

Dr. Leathart is not alone among recent authors to refer to asbestos bodies (see J. C. GILSON in *Modern Trends in Occupational Health*, Ed. by R. S. F. SCHILLING, London, 1960, Butterworths Modern Trend Series, p. 63). The original term was introduced by M. J. STEWART and A. C. HADDOW in an article entitled *Demonstration of the Peculiar Bodies of Pulmonary Asbestosis* ("*Asbestosis Bodies*") *in material obtained by Lung Puncture and in the Sputum* [this *Bulletin*, 1930, v. 5, 247]. There may be sound reasons for this change in nomenclature but some authority ought to present a reasoned exposition of the subject so as to establish a standard usage.]

Part 2 on pulmonary function tests carried out over several years in the 10 cases of asbestosis is a very important contribution to the subject. Diminution in values as compared with the controls was observed for diffusing capacity for carbon monoxide (Dco), pulmonary compliance, maximum voluntary ventilation and vital capacity. The author suggests that the demonstration of a progressive decline in vital capacity or in diffusing capacity may enable a diagnosis of asbestosis to be made before radiological abnormality has appeared but states that this point has not been proved.

[This physiological approach may have a wider application in the investigation of such dusts as talc and mica. In essays on asbestosis it is not sufficiently underlined how much the pleural changes dominate and determine the clinical, radiological and morbid anatomical manifestations. Many physicians have remarked that on the basis of rigidity of the chest, dyspnoea, clubbing of the fingers and earthy cyanosis, asbestosis is a clinical rather than a radiological disease.] *A. Meiklejohn*

SZYMCZYKIEWICZ, K. Wpływ długości włókien azbestu (chryzotylu) na rozwój włóknistych zmian w płucach świnek morskich. [**The Effect of the Length of Asbestos Fibres (Chrysolite) on the Development of Fibrous Changes in the Lungs of Guinea-Pigs**] *Med. Pracy*. 1960, v. 11, No. 3, 145–66, 8 figs. on 6 pls. [68 refs.]

The English summary appended to the paper is as follows:—

"Two groups of guinea-pigs (10 animals in each group) were treated with fibrous asbestos dust (chrysolite) intratracheally. The first group was treated with short-fibre dust (geometric mean 4.0 μ), the second with long fibre dust (geometric mean 10.8 μ). 10 mg of dust were administered 6 times every two days. Each guinea-pig received 60 mg of dust together.

"One group of animals was killed with aerial emboli 6 months, and the other 12 months after dust administration.

"The lungs of the animals were cut up into blocks for histological section. Five paraffin sections were made, one each for haematoxylin and eosin staining according to Van Gieson, Gomori and Gloyne.

"The results were worked out statistically by comparing the section from each group in which the analogical changes have been observed. Some sections were incinerated and examined by polarizing microscope. Other sections were examined by electronic microscope. Crystals found in preparations were submitted to the electronic diffraction.

"On the ground of these investigations it seems that asbestos dust, containing the greater percentage of longer fibre particles, is more noxious because it provokes more extensive and distinct reaction: in bronchi, in peribronchial tissue and in pleura.

"Investigations carried out with the use of electronic microscope and microincineration have showed that the asbestos dust did not dilute completely during the 12 months period of resting in the lungs. Nevertheless, in the crystalline structure of the dust some changes occur which can result from progressive dissolution of asbestos."

BALDUS, W. P. & PETER, J. B. **Farmer's Lung: Report of Two Cases.** *New England J. of Med.* 1960, Apr. 7, v. 262, No. 14, 700–705, 4 figs. [17 refs.]

These authors, from Minnesota, describe 2 cases of farmer's lung and discuss their findings in relation to observations on this condition recorded by previous authors.

The first case was that of a farmer aged 39 years. On admission on March 26, 1959, he complained of attacks of shortness of breath which occurred intermittently since late January of that year. He did not complain of any other respiratory symptoms, but admitted to producing small amounts of pale yellow sputum daily. During his attacks of dyspnoea his temperature rose to a maximum of 101°F. He was also suffering from anorexia and had lost about 10 to 15 lb. in weight.

His past history revealed that he had been exposed for most of his life "to dust, hay, silage, and chickens," and had, despite this, been "in perfect health". In 1958 he was exposed for the first time to mouldy fodder.

On physical examination this patient did not present with any remarkably abnormal respiratory features, but X-ray examination revealed "a diffusely reticular and finely nodular pattern, with lesions of about 2 mm. in diameter scattered throughout both lung fields". Laboratory findings were not remarkable.

Shortly after admission the patient recovered his previous health and agreed an April 7 to inhale dust from mouldy hay. As a result of this, the patient experienced "the sudden onset of nasal congestion, a single chill, increasing productive cough and marked shortness of breath". These respiratory disturbances persisted for several days.

Biopsy sections from the lungs showed "small parenchymal granulomas in which giant cells were the predominant feature". No other abnormalities and no organisms were detected in this material.

The second case was of a farmer aged 45 years who, on March 19, 1956, gave a history of "sudden onset of productive cough, shortness of breath, weight loss and fever in November, 1955". He recovered to some extent after treatment. He claimed that his respiratory symptoms were precipitated by exposure to dust while at work in his barn, and these were most severe during the winter.

On April 14, 1959, after attending the outpatients department for several years, he submitted to operation for the purpose of providing biopsy material. Sections from this revealed, as in the previously described case, granulomas with giant cells, but no organisms were seen and none recovered on culture.

These findings are in the main consistent with many of those reported by other authors writing on this subject [this *Bulletin*, 1958, v. 33, 1054; 1960, v. 35, 18].

C. J. La Touche

MEICHEN, F. W. **Modern Welding and Health Hazards.** *Trans. Ass. Indust. Med. Officers.* 1960, July, v. 10, No. 2, 39–44, 2 figs. [18 refs.] Discussion 44–5.

This paper describes an environmental and clinical study in two quite separate workshops in which welding of aluminium and stainless steel was being carried out by the inert-gas shielded-arc process. Air sampling was carried out at various situations within the workshops for metal fumes and ozone and the results of these tests are presented in tabular form. Ozone concentrations ranged from 0·01 p.p.m. at 6 ft. to 168 p.p.m. close to the arc but within this range there was a wide scatter of concentrations at distances from the arc of 6 in. to 45 ft. Analysis of the atmospheric samples for metal impurities demonstrated the presence of aluminium, iron, lead, manganese, calcium and nickel but no solvents were detected.

A number of the employees in the workshops were interviewed and some of them complained of an unusual odour, dryness and roughness of the throat, constriction of the chest which usually developed a day or two after exposure began, and a dislike for smoking. Some typical case histories are quoted in the paper and there is a brief review of the toxicology of ozone.

In the discussion mention is made of the similarities and certain differences between the investigation reported in the above paper and that described in a paper by CHALLEN *et al.* [this *Bulletin*, 1959, v. 35, 247]. There seems to be no doubt about the toxicity of ozone, for animal experiments have amply confirmed this, but the production of ozone in welding may present more complex problems than exposure to it under laboratory conditions. Ozone could be adsorbed onto metal fume particles, or in certain circumstances residual trichloroethylene on the metallic components to be welded could combine with small amounts of nitric oxide or nitrogen dioxide to give a chlorinated, conjugated nitro-olefin. Nitro-olefins are highly toxic substances.

P. J. R. Challen

PEGUES, W. L. **Lead Fume from Welding on Galvanized and Zinc-Silicate Coated Steels.** *Amer. Indust. Hyg. Ass. J.* 1960, June, v. 21, No. 3, 252–5.

There is an increasing use in industry, particularly in ship building, of coatings for steel plate which are applied for their anti-corrosive properties prior to welding or oxy-acetylene cutting. The author of this paper was interested in the modern zinc-silicate applications and steel which had been through the hot-dipped galvanizing process, and he investigated the possibility that welding and cutting of steel with these coatings might give rise to hazardous amounts of lead and zinc fumes. The investigation was carried out in 2 large well-ventilated buildings and in an enclosure 6 by 10 feet, open at the top, which was designed to represent a confined space. Air samples were taken at various distances from the welder, including from his breathing zone, and the results of these tests are tabulated in detail.

Results of the investigation show that at the welder's breathing level welding or cutting operations on steel having a zinc-silicate coating in poorly ventilated areas gave rise to fumes containing 4 to 75 times the maximum allowable concentrations of lead and 1 to 14 times the MAC of zinc. The same operations on galvanized steel under similar conditions produced fumes containing 2 to 4 times the MAC of lead, and 3 to 12 times the MAC of zinc. When ventilation was adequate the MAC was not greatly or consistently exceeded for either type of metal coating.

P. J. R. Challen

ROSS, C. R., WINDISH, J. P., DUBOIS, L., MONKMAN, J. L. & DE VILLIERS, A. J. **Survey of Lead Hazard in Indoor Firing Ranges.** *Amer. Indust. Hyg. Ass. J.* 1960, June, v. 21, No. 3, 256–60, 2 figs.

Recent publications have drawn attention to a lead hazard in firing ranges under conditions of poor ventilation. Airborne lead in these ranges is generated in 3 ways; by combustion of the lead compounds usually found in priming compositions, by abrasion of the bullet when it leaves the gun, and by fragmentation of the bullet when it strikes the target or backstop. Following the discovery of lead poisoning in an instructor at an Ottawa firing range in 1957 the authors carried out air sampling for lead in this range and at 6 others in different parts of Canada, together with ventilation measurements and analyses of urine samples for lead content. About 100 air samples and 130 urine samples were analysed for lead. Air samples were collected at breathing level before, during, and after, various firing procedures with an electrostatic precipitator and a millipore filter aerosol sampler. Urine samples, about 200 ml. each, were collected off the range on the first Friday of each month and persons were asked to report the number of hours they had spent on the range during the previous month and how much ammunition they had fired during those periods.

The results of the air sampling programme revealed concentrations of lead many times in excess of the maximum allowable concentration. However, the urine results were all, with the exception of one individual, below 150 μgm. per litre, the latter concentration being the maximum safe limit. The discrepancy between the high air concentration of lead and the low urinary excretion levels is explained on the basis of the discontinuous exposure of most of the individuals [this *Bulletin*, 1959, v. 34, 785]. Control measures were recommended because of the high air concentrations of lead and because 3 individuals showed heavy absorption

during the previous 2 years. For the individual range a supply of tempered fresh air with some form of draughtless distribution over the firing end was recommended plus exhaust ventilation from the target end. In addition to good ventilation firing ranges should maintain good housekeeping standards in order to prevent contamination caused by redispersal of settled dust.

P. J. R. Challen

GRANDJEAN, E. & WÜTHRICH, M. Untersuchungen über die Bleigefährdung von Spleissern. [**Risk of Exposure to Lead Workers in Cable Laying**] *Zent. f. Arbeitsmed. u. Arbeitsschutz.* 1960, July, v. 10, No. 7, 153–8.

Telephone cables are supplied by the manufacturers in lengths of 200 metres which after being laid in the ground must be joined together by a method known as *spleissen* which is here described shortly. It includes the soldering together of the component wires of each length of cable to those of the next length and covering the join with a muff which contains 72% of lead. The workers of this method are exposed to lead fumes and lead dust.

This paper contains the results of chemical determination of the lead concentration of water after use by the workers to wash their hands and of the lead content of the air under different conditions. 50 of the workers were examined clinically. The lead content of the urine was determined and blood examination for haemoglobin concentration and the presence of punctate basophilia was carried out. The history of sickness of these workers and their subjective symptoms were investigated.

The main conclusion is that these workers are exposed to a certain risk from exposure to lead but that the results of the clinical investigation of the group of men do not warrant a diagnosis of lead intoxication in any instance. It is considered that the good instruction of the workers and their personal cleanliness are responsible for the very small intake of lead which tests revealed and for the comparatively good state of health of the whole group.

M. E. Delafield

BATTIGELLI, M. C. **Mercury Toxicity from Industrial Exposure. A Critical Review of the Literature. Parts I & II.** *J. Occup. Med.* Chicago. 1960, July & Aug., v. 2, Nos. 7 & 8, 337–44; 394–9. [101 refs.]

MED. D. LAVORO. 1960, May, v. 51, No. 5, 389–92. **Resolutions of the International Symposium on Maximum Allowable Concentrations of Toxic Substances in Industry, Prague, 14–17 April 1959.**

ARCH. ENVIRONMENT. HEALTH. Chicago. 1960, Aug., v. 1, No. 2, 140–44. **Threshold Limit Values for 1960. Adopted at the 22nd Annual Meeting of the American Conference of Governmental Industrial Hygienists, Rochester, New York, April 23–26, 1960.**

WIRTSCHAFTER, Z. T. & BISCHEL, Margaret G. **Reticuloendothelial Response to Benzene.** *Arch. Environment. Health.* Chicago. 1960, July, v. 1, No. 1, 10–16, 5 figs.

This is an illustrated description of serial imprints which revealed cellular changes during the week after a minimal subcutaneous injection of benzene, 0·4 ml. per kgm., in rats. [See also this *Bulletin*, 1960, v. 35, 548.] The reticuloendothelial (RE) response occurred in marrow, lymph nodes, thymus and spleen, and the normal imprint appearance of each tissue is described first. Numerical values for various cells in serial marrow imprints appear in a table beside those obtained after injection of carbon tetrachloride. Both substances produced aberrations of different degree or kind in the haemopoietic system, which had not returned to normal at the end of the study.

In the marrow the intensity of the RE response to benzene took 72 hours to reach its peak and RE cells remained present in numbers approximately twice the mean normal value. Giant cells of foreign body type appeared in the 2-hour imprint. Atypical megakaryocytes appeared in 2 hours, and from 10 to 120 hours there was decreased thrombocyte formation. In lymph nodes and thymus, RE cells of the macrophage type increased at 16 hours and gradually decreased to normal numbers by 7 days. The spleen showed persistent proliferation of RE cells of the pulp-cell type with morphological changes. No abnormalities were seen in liver imprints, and blood counts remained normal.

M. Patricia Fitzsimons

HAKE, C. L., WAGGONER, T. B., ROBERTSON, D. N. & ROWE, V. K. **The Metabolism of 1,1,1-Trichloroethane by the Rat.** *Arch. Environment. Health.* Chicago. 1960, Aug., v. 1, No. 2, 101–5.

"After intraperitoneal injection into the rat, 1,1,1-trichloroethane-1-C^{14} was rapidly and almost totally excreted via the respiratory system. When doses of near 700 mg/kg. were given to three animals, 98.7% of the dose could be accounted for as unchanged 1,1,1-trichloroethane-1-C^{14} in the expired air. One-half of one percent of the dose was converted to $C^{14}O_2$, while much of the remainder appeared as the glucuronide of 2,2,2-trichloroethanol-2-C^{14} in the urine. It is concluded that the favorable toxicological picture found upon both acute and chronic vapor exposures of animals to 1,1,1-trichloroethane is due to the ability of the animal to excrete the chemical rapidly and almost totally via the respiratory system."

GRANDJEAN, E. **Trichloroethylene Effects on Animal Behavior. The Effects of Trichloroethylene Vapors on a Food Motivated Conditioned Climbing Reaction of Rats.** *Arch. Environment. Health.* Chicago. 1960, Aug., v. 1, No. 2, 106–8, 2 figs.

"We have studied the effects of exposure to trichloroethylene vapor on rats conditioned to climb up a rope in order to reach a feeding trough where they found a

reward (sugar pellet). Previous exposure to 200 and 800 ppm of solvent did not modify either the conditioned responses or the response time of the animals.

"On the other hand, the spontaneous climbs (without previous signals) were significantly more frequent with the rats exposed than with the controls. This observation permits the conclusion that trichloroethylene in the doses studied modifies the psychological equilibrium of rats in the sense of a disinhibition or of an increased excitability."

McNerney, J. M. & Schrenk, H. H. **The Acute Toxicity of Cyanogen.** *Amer. Indust. Hyg. Ass. J.* 1960, Apr., v. 21, No. 2, 121–4, 1 fig. [10 refs.]

Little experimental work has been reported on cyanogen toxicity. Conflicting comparisons have been made with hydrogen cyanide and various reviews have inaccurately expressed early data. This study indicates that the gas cyanogen, NCCN, also referred to as oxalic nitrile, ethane dinitrile or prussite, is less toxic than HCN.

Several groups of rats were exposed to 6 different concentrations of cyanogen for 6 different periods. Mortality data are given in a table and, calculated as LC50, are graphically presented on a log-scale which delineates areas of total, partial or no mortality at concentrations ranging from 250 to 2,000 p.p.m. Mortality ratios were:

Mortality	Concentration	Period
0/6	2,000 p.p.m.	7·5 minutes
	1,000 „	15 „
	500 „	30 „
	400 „	45 „
	250 „	60 „
6/6	4,000 „	15 „
	2,000 „	15 „
	1,000 „	30 „
	500 „	45 „
	400 „	60 „
3/6	4,000 „	7·5 „
4/6	250 „	120 „

The 2 survivors of the last group died during the 14-day holding period, the first after 7 hours with central nervous symptoms, the other after 7 days with no apparent symptoms; these were the only delayed deaths.

Effects observed during exposures included asphyxia, lachrymation, upper respiratory tract irritation, pink skin, accentuated, poorly co-ordinated movements or tremors and prostration.

In skin absorption tests rabbits showed no effects from exposure of the clipped body, except the head, to 10,000 p.p.m. for 8 hours. At autopsy neither rabbits nor rats showed gross changes.

Human subjects exposed to 16 p.p.m. for 6 or 8 minutes experienced eye and nasal irritation—(but not at 8 p.p.m.)—and so did another exposed for 6 minutes to the resulting concentration after the first group. Odour was not detected in these tests, nor in tests with sampling tubes connected to a chamber containing 50–250 p.p.m.

M. Patricia Fitzsimons

Estes, Frances L. & Gast, J. H. **The *in vitro* Effects of Aliphatic Nitro Compounds on Tissues.** *Arch. Environment. Health.* Chicago. 1960, July, v. 1, No. 1, 47–52, 4 figs. [12 refs.]

A preliminary report of the examination of the effects of alkyl nitro compounds on metabolic processes was presented in 1958 to the American Society of Biological Chemists. The oxygen consumption of leucocytes and of homogenates of heart and liver from guineapigs was determined in the presence and absence of aliphatic nitro hydrocarbons. Tissue respiration was inhibited by the shorter chain compounds, saturated (C_1–C_3) and unsaturated (C_3), at low concentrations.

One of the problems of applying *in vitro* techniques to the study of the biochemical effects of volatile substances involved the measurement of oxygen consumption while the substance itself was contributing to the vapour phase, and several procedures are pointed out which demonstrate the validity of the results. These are included in some of the tables and figures. As the concentration of the nitro compounds was increased the oxygen consumption passed through a minimum and increased with further increase of the concentration. The oxygen consumption observed at both low and high concentrations suggests that at least 2 reactions are involved.

M. Patricia Fitzsimons

Rinehart, W. E., Donati, E. & Greene, E. A. **The Sub-Acute and Chronic Toxicity of 1,1-Dimethylhydrazine Vapor.** *Amer. Indust. Hyg. Ass. J.* 1960, June, v. 21, No. 3, 207–10. [14 refs.]

A certain number of studies have been carried out on the acute toxicity of 1,1 dimethylhydrazine (UDMH) [this *Bulletin*, 1956, v. 31, 547; 1957, v. 32, 1071] which is being used in guided missile systems, but studies of longer duration are needed to estimate the quantity of that toxicant to which man may be exposed without harmful effects. This paper reports an investigation in which rodents were exposed to 140 p.p.m. of 1,1 dimethylhydrazine vapour for 6 weeks and to 75 p.p.m. for 7 weeks. Dogs were exposed to 25 p.p.m. for 13 weeks and to 5 p.p.m. for 26 weeks.

At the high concentrations dogs and rodents developed tremors, convulsions, and then died; at the low concentrations they showed lethargy, some dyspnoea and evidence of haemolytic anaemia. The dogs were significantly more sensitive than the rodents. Pathological studies of the liver, spleen, lymph nodes and bone marrow in dogs supported the diagnosis of haemolytic anaemia.

On the basis of the results of these studies the authors suggest a maximum allowable concentration of 0·5 p.p.m. for human exposure and they conclude that lethargy and haemolytic anaemia would be the first toxic signs to appear.

P. J. R. Challen

Mendenhall, R. M. **Measurement of Ketene for Study of its Toxic Action on Animals.** *Amer. Indust. Hyg. Ass. J.* 1960, June, v. 21, No. 3, 211–18, 7 figs. [11 refs.]

This detailed paper presents an analysis of experimental variables encountered during long-term studies of ketene

toxicity. Apparatus for the generation, metering and measurement of the gas is illustrated. The method of analysis of DIGGLE and GAGE, depending upon the reaction with hydroxylamine and the formation of a coloured complex with ferric ion, was satisfactory for high concentrations, but it was modified for low concentrations to avoid variables caused by heating. To select the least wasteful control analytical procedure, 4 general mathematical methods were tested on the results of 48 analyses of exposure chamber samples. A table of differences between these methods is followed by a figure of the differences between the values for 1 sample. This test showed that a single standard curve should not be used; the equation of a standard curve of at least 3 points determined concurrently with each unknown would be best, but when 1 known standard was included in the analysis the results were within acceptable limits.

The concentration of ketene in various parts of the 100 cu.ft. exposure chamber is shown in a figure to be uniform, and 1 test daily was found adequate. The gases from the generator were delivered to give a calculated concentration of 2·39 p.p.m. ketene in the exposure chamber, but the average of 200 chamber measurements was 1·02 p.p.m. The rate of alteration of ketene was measured. Moisture was found to affect exponentially the rate of conversion to the dimer, but this effect had no significance in these studies, and an experiment to test the effect of a metal catalyst, Hg vapour, did not increase this rate. *M. Patricia Fitzsimons*

PAUL, J. & POVER, W. F. R. **The Failure of Absorption of DC Silicone Fluid 703 from the Gastrointestinal Tract of Rats.** *Brit. J. Indust. Med.* 1960, Apr., v. 17, No. 2, 149–54. [22 refs.]

Various silicones are used for lubricating surgical appliances and baking pans and as antifoaming agents in the manufacture of sugar, beverages, chewing gum, drugs and cosmetics. The absence of harmful effects may have been due to failure of absorption or rapid elimination. In order to be absorbed, some lipid-like materials need to be dissolved in a triglyceride vehicle. In this study a methylphenyl polysiloxane (703) was chosen because of its lipid-like character and its solubility in olive oil. The methyl polysiloxanes are insoluble.

Rats, after starvation, were given solutions of 703 in olive oil by oral intubation. Results of administration of 703, lipid or silicone extractions are given in tables and biased errors are considered. After cannulation of the intestinal lymphatic duct, 0·65 ml. of a 15% solution in olive oil, coloured by β-brown which is absorbed by the lymphatics, was given, and chyle was collected every 3 hours. Other rats were killed 3½ hours after being given 0·65 ml. of 18·3% or 25·6% solutions; the gastrointestinal tract, after ligature of stomach and caecum, was removed and the lipid contents were extracted. In an 8-day experiment the diet contained 4% 703 and 16% oil; urine and faeces were collected daily; afterwards lipid and lipid-soluble materials from the gastrointestinal tract were extracted, and also the lipid content of each liver, kidney and fat depot.

The coloured lymph contained no silicone. In the 3½ hours' experiment, 85% of the 703 was in the gastrointestinal tract, none in the homogenized intestinal mucosa, and 70% of the oil was absorbed. The 8-day experiment gave recoveries of 96% of the silicone, entirely from the lower intestine and faeces; none was found in liver, kidneys or fat; the urine contained no silica.

The failure of absorption of this silicone and the simultaneous absorption of the triglyceride vehicle imply a mechanism in the intestine which actively separates the intimately mixed substances which are of similar particle size. This mechanism is being investigated. [See also this *Bulletin*, 1960, v. 35, 972.]

M. Patricia Fitzsimons

AGNOLETTO, A. Su di un caso, a insolito decorso, di fistola vescico-intestinale, secondaria a neoplasia vescicale da beta-naftilamina. [**On an Unusual Case of Bladder-Intestine Fistula from Bladder Cancer due to Beta-naphthylamine**] *Med. d. Lavoro.* 1960, May, v. 51, No. 5, 385–8.

The English summary appended to the paper is as follows:—

"A case of bladder-intestine fistula derived from a bladder tumour due to beta-naphthylamine is described. The main observations are based on the etiopathogenetic mechanism: the fistula derives from the neoplasm which has an occupational origin; the fistula appeared after a treatment with hard gamma rays from a cobalt bomb. Clinical observations include the one-way function of the fistula from bladder to intestine (which allowed a perfect compensation of renal excretory activity and even removed a previous increase in blood nitrogen) and anuria for over 40 days."

SUTTON, W. L., TERHAAR, C. J., MILLER, F. A., SCHERBERGER, R. F., RILEY, E. C., ROUDABUSH, R. L. & FASSETT, D. W. **Studies on the Industrial Hygiene and Toxicology of Triphenyl Phosphate.** *Arch. Environment. Health.* Chicago. 1960, July, v. 1, No. 1, 33–46, 2 figs. [25 refs.]

Because of the resemblance in chemical structure shown by triphenyl phosphate (TPP), and tri-ortho-tolyl [tri-ortho-cresyl] phosphate (TOTP), the toxicity of the 2 substances is discussed and the literature summarized. In these studies the animal experiments with TPP extend toxicological data to the rat, mouse and guineapig, and the environmental studies give a quantitative evaluation of exposures of men working with TPP.

The oral and subcutaneous acute toxicity in the rodents was low: no signs or deaths from 3·0 gm. per kgm. Cholinesterase activity was used as an indicator of absorption. In mice, oral and intraperitoneal administration caused cholinesterase inhibition directly related to the dose of TPP; by inhalation a small portion was absorbed; none was absorbed through the skin which was not irritated by 0·5 ml. of an alcoholic solution. Though TPP inhibited cholinesterases *in vivo* and *in vitro*, large doses did not produce cholinergic symptoms in rats, mice, guineapigs or cats. In some of the cats intraperitoneal injection of 0·2 or 0·4 gm. per kgm. was

followed 18 and 16 days later by paralysis and general illness; other cats remained symptom-free after doses up to 0·3 gm. per kgm., though one died 3 days after this dose of a perforated gastric ulcer. When administered orally or subcutaneously to the rodents, TPP was slowly absorbed; some was found at the administration sites a month later.

In 35-day feeding experiments in rats, the diet contained 0·1% TPP; no haematological changes occurred and no gross abnormalities were found at autopsy. Preliminary experiments with 0·5% had caused food refusal, and liver weights were greater than in those of controls.

In men exposed for as long as 10 years to TPP vapour, mist or dust, at a weighted average concentration of 3·5 mgm. per m.^{3}, there was no evidence of adverse clinical effects. In the men engaged in manufacture of TPP a significant reduction of red blood cell cholinesterase activity was found; this probably represented an effect of TPP absorption. *M. Patricia Fitzsimons*

BRUAUX, P. Prévention des intoxications par les organophosphorés. **[Prevention of Poisoning by Organic Phosphates]** *Bull. World Health Organization.* Geneva. 1960, v. 22, No. 5, 575–8.

This is a report from the Belgian Congo on the blood cholinesterase levels determined by the DAVIES and NICHOLLS method in a considerable number of men engaged in work with the organic phosphates diazinon, malathion and Dipterex. From the results of this investigation it is concluded that although these insecticides have a relatively feeble acute toxicity their chronic toxicity for man is not negligible. It is accordingly proposed that certain preventive measures which are outlined should be introduced. These measures are based on regular determinations of blood cholinesterase levels and alternations in the periods of work in which after 2 months' work with these insecticides there should be 2 months of employment not entailing exposure to these chemicals. *M. E. Delafield*

PLOEM, J. E. & SMIT, G. J. F. Parathionvergiftiging van een beheel gezin na gebruik van verse groenten. **[Parathion Poisoning of an Entire Family from eating Fresh Vegetables]** *Nederl. Tijdschr. v. Geneesk.* 1960, Aug. 27, v. 104, No. 35, 1663–4.

English summary appended to the paper is as follows:—

"Report on a family with severe symptoms of poisoning caused by eating spinach tainted with parathion. The spinach had been kept in a gunny sack which was found to contain parathion."

TRACY, R. L. **Insecticidal and Toxicological Properties of DDVP.** *Soap.* New York. 1960, July, v. 36, No. 7, 74–6, 105. [11 refs.]

In a review of the uses of *O,O* dimethyl 2,2-dichlorovinyl phosphate (DDVP) the author describes results obtained in the laboratories of the Norda Essential Oil and Chemical Co., New York.

DDVP applied at the rate of 0·5 mgm./ft.^{3} killed house and stable flies in 2–5 hours but the dose had to be increased to 2 mgm./ft.^{3} to kill cockroaches and cigarette beetles within 18 hours.

The LD50 of pure DDVP applied to the intact rat conjunctivae was 10 mgm./kgm. In cattle 9 gm. DDVP applied daily to the skin for 10 days did not lower the erythrocyte cholinesterase level. Oral doses which depressed the blood cholinesterase levels of female rats and cows did not affect the level in the suckling young

DDVP is inactivated by the liver. *H. B. Stoner*

U THAN PE & VENKAT RAO, V. **Dieldrin Spraying Operations in the Arakan Region of Burma, with special reference to Precautions taken against Toxic Hazards.** *Bull. World Health Organization.* Geneva. 1960, v. 22, No. 5, 582–4.

In 1951 malaria control operations were begun in the Arakan region of Burma by the Government of the Union of Burma in collaboration with the Economic Cooperation Administration mission of the United States Government. The method of control adopted was annual indoor residual spraying with technical DDT in water suspension at a dosage of 2 gm. per square metre. Routine susceptibility tests in 1957 indicated that *Anopheles sundaicus*, which from evidence was considered to be important enough to be included in the list of local vectors, had developed a marked increase in its tolerance to DDT though still susceptible to dieldrin. Dieldrin at a dosage of 0·5 gm. per square metre therefore replaced DDT in the annual sprayings. As dieldrin is toxic to spray-men and some domestic animals [this *Bulletin*, 1959, v. 34, 1270], strict enforcement of precautionary measures was essential. A detailed statement of these measures is given and these included the supply of protective clothing, instruction of staff and insistence on personal hygiene. Details of the spray campaigns in 1958 and 1959 are given in a table and it is reported that in these 2 years there have been no cases of poisoning among the spray-men and no casualties in domestic animals. *M. E. Delafield*

KLEINMAN, Goldy D., WEST, Irma & AUGUSTINE, Marguerite S. **Occupational Disease in California attributed to Pesticides and Agricultural Chemicals.** *Arch. Environment. Health.* Chicago. 1960, Aug., v. 1, No. 2, 118–24.

In California the number of reported cases of occupational disease attributed to pesticides and agricultural chemicals has risen from 400 per year in 1951 to 749 in 1957. This paper gives an analysis of the cases reported in 1957. Notification of occupational illness is required by law in California and the data given in the paper are derived from more than 90% of the agricultural labour force. Nearly a third of the 749 cases were attributed to organo-phosphorus insecticides. The authors conclude that agricultural chemicals and particularly this group are becoming an increasingly important public health problem and that there should be more education in their safe use. *H. B. Stoner*

WILSON, H. T. H. **Rubber-Glove Dermatitis.** *Brit. Med. J.* 1960, July 2, 21–3, 6 figs. [13 refs.]

Numerous cases of skin sensitivity to rubber have been reported [this *Bulletin*, 1933, v. 8, 335; 1952, v. 27, 1042] and these have been mainly allergic dermatitis of the hands. Here reported are 42 patients, 38 females and 4 males, who suffered from dermatitis of the hands; of these, 17 had had no skin trouble before wearing rubber gloves and 13 had started to wear them because of a rash attributed to detergents. Other sites were affected in 22 patients from contact with the elastic of hairnet, face-mask, brassiere, suspenders, rubber-topped socks, Plimsoll shoes and adhesive plaster.

There is an account of the manufacture of rubber gloves in which before vulcanizing the rubber, chemicals known as accelerators and other chemicals including antioxidants are employed. An extensive series of patch tests were carried out on the 42 patients not only with patches of household and of surgical glove material but also with a number of the chemicals used in manufacture. A table sets out the results of these tests. The main results were that (1) of 42 patients tested 37 were sensitive to household gloves, (2) of 35 tested with surgical gloves only 4 were positive and (3) all but 2 of the patients were sensitive to 1 or more of the chemical accelerators. The highest percentages of positives to these chemicals were 71·43% to dipentamethylene thiuram disulphide, 47·62% to tetramethyl thiuram disulphide and 35·71% to mercaptobenzthiazole.

M. E. Delafield

MORRIS, G. E. **Dermatoses from Phenylmercuric Salts.** *Arch. Environment. Health.* Chicago. 1960, July, v. 1, No. 1, 53–5, 2 figs. [14 refs.]

"Sensitivity to phenylmercuric salts must be considered when people develop eruptions of the legs after spreading weed or crab-grass killers; the eruption may also appear on the hands from handling the product.

"Sensitization dermatitis in other body areas may be due to a phenylmercuric salt being used as a primary antiseptic, as a preservative in ointments, or as a spermicidal agent in contraceptive jellies."

FELTON, Jean S. & ROZAS, C. J. **Decontamination of Human Skin experimentally soiled by Radioactive Materials.** *Arch. Environment. Health.* Chicago. 1960, Aug., v. 1, No. 2, 87–95, 2 figs.

It is extremely difficult to rid the hands of a radioactive contaminant — witness the number of papers on the subject in recent years. The authors have made a detailed study not only of detergents but of the technique which should be brought into play in removing the contaminant. Scrubbing with soap and hot water may render the skin more absorbent when once again brought into contact with radioactive material. The technique is described in detail with a list of granulated skin cleaners and waterless skin cleaners; the contaminants were the radioactive isotopes of iodine and phosphorus. With the best of the cleansers a very high degree of removal was obtained. These are listed in footnotes for the benefit of potential users.

[The article should prove of considerable practical value.] *S. Russ*

LABELLE, C. W., BRIEGER, H., GODDARD, J. W., RASTATTER, K. A. & ZINGER, B. L. **Retention and Effect of Radioactive Particulates in the Lung.** *Amer. Indust. Hyg. Ass. J.* 1960, June, v. 21, No. 3, 195–200, 2 figs.

In the course of this article certain terms are given a precise meaning in their application. *Deposition* concerns the transfer of suspended particles from the air to the inner surfaces of the lungs during the process of respiration. *Retention* refers to the time interval during which this material remains in the lungs after it is deposited. *Lung burden* is the amount of material present in the lung at any given instant of time. *Clearance* is the rate at which the lung burden decreases as a result of transport to other regions of the body or of elimination from the body by the excretory mechanisms. Three criteria are necessary for the estimation of a maximum permissible concentration of a radio-isotope in the environment: the critical organ and its critical burden must be known and the quantitative relation between environmental concentration and corresponding organ burden must be estimated. The critical organ is the one which coresponds to the lowest critical environmental concentration. The lung is an important organ in this respect for while it may itself be the critical organ it may become a reservoir from which small concentrations of an isotope are maintained over long periods and thus affect peripheral organs.

The authors have studied the effects of injections of foreign particulates into the lungs of rats. Activated uranium dioxide was used in physiological salt solution. A single dose was given and rats were killed at intervals for assay of lung content of the uranium. It is eliminated in two stages; during the first stage about one-third of the material within the first day or two, while the remainder is eliminated much more slowly with a half-life of 73 days.

The authors compare their findings with those of MORGAN *et al.* (*Proceedings of the International Conference on the Peaceful Uses of Atomic Energy*, v. 13, pp. 139–158. 1956, New York: United Nations) and point out the probable reasons for discrepancies.

S. Russ

BLANCHARD, R. L. & HOLADAY, D. A. **Evaluation of Radiation Hazards created by Thoron and Thoron Daughters.** *Amer. Indust. Hyg. Ass. J.* 1960, June, v. 21, No. 3, 201–6, 4 figs. [14 refs.]

[To many English readers the term "daughter" applied to any radioactive substance is a misnomer; there are no sons or daughters, only descendants. The excellent descriptive term "active deposit" was coined in the Curie-Rutherford days and has since been used in most physical writings. But some American writer thought he could do better and call the successive products of

radon and thoron "daughters". So we meet this term once again and the authors write on methods of measuring atmospheric concentrations of thoron daughters.]

The chief steps outlined for this purpose are:—

1. Draw a known quantity of the contaminated air through a filter paper (50–100 litres).
2. After sampling, allow the filter sample a minimum of 5·6 hours to reach equilibrium. Then determine the number of alpha ray disintegrations per minute by using a calibrated detecting instrument.
3. The working level is then determined by multiplying the number of disintegrations per minute by the working level factor given in Fig. 3 of the text.

There is a growing use of thorium in industry and the chief source of danger to operatives is in the inhalation of thoron. *S. Russ*

POWELL, M. **The Hazard of Strontium-90.** *Irish J. Med. Sci.* 1960, Aug., 6th Ser., No. 416, 363–71, 1 diagram. Discussion 371–3.

To quote from the author of this exceptionally valuable paper, "when a nuclear weapon explodes, the first thing seen is an immense ball of fire, more brilliant than the noon-day sun and visible more than 400 miles away. Immediately, it expands and rises like a gigantic hot-air balloon at a speed of about 300 miles an hour. One minute after the explosion, the fireball is already 5 miles high. . . . As the radio-active cloud rises, some of the materials in it are caught by the winds and fall to earth. This is local fall-out, the concern of the civil defence worker and an immediate problem. It falls over an area whose shape depends on the prevailing winds, but which is generally regarded as having the outline of a cigar about 150 miles long and 25 miles wide."

Something like one-half of the total fission products is projected into the stratosphere; here they may be retained for some years. It has been found that irrespective of the locality of the explosion most of this radioactivity comes to lie in a band which circles the world in the temperate zone at about 30–60° N. lattitude. Rainfall is mainly the cause of its deposition on the eartn. At fission there are two groups, "light" and "heavy", and the present article is concerned with the deposition of the "light" group—Strontium 89 and Strontium 90.

Strontium 90 is the more important because of its comparatively long life (effective half-life $2{\cdot}7 \times 10^3$ days). It emits beta rays and is selectively absorbed by bone; hence its danger once it is absorbed into the body.

Strontium 90 is chemically allied to calcium and it moves with this element through the food chains and the foods which supply calcium to the body also supply Strontium. In fact, exposure of the population occurs primarily by the contamination of dietary calcium by Strontium 90. In this work a study is made of the Strontium 90–calcium ratio in the food chains and in the final deposition in the body.

The author quotes data from the Agricultural Research Council of Britain's Report on the contamination of food by Strontium 90 (1958–59). This article is one in which every paragraph is worth the reader's attention. *S. Russ*

KULP, J. L., SCHULERT, A. R. & HODGES, Elizabeth J. **Strontium-90 in Man. IV. The Strontium-90 Concentration in Human Bone increased in 1958 and 1959, will probably reach a Maximum in 1960.** *Science.* 1960, Aug. 19, v. 132, 448–54, 3 figs. [Numerous refs.]

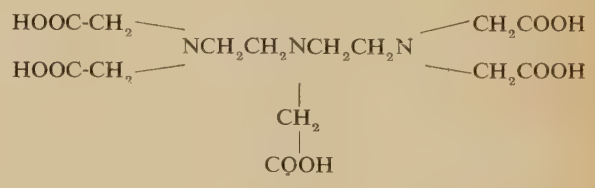
This article contains both fact and prophecy as to strontium 90 in the body. It is higher today than it used to be, but it may become lower if wisdom prevails over atomic bombs.

This is an exhaustive study as may be gathered from the statement that since the beginning of this study in 1953 (*Science*, 1957, v. 125, 219; 1958, v. 127, 266; 1959, v. 129, 1249), some 9,000 samples of human bones have been procured—single bone samples of people of all ages, whole skeletons and foetuses. The actual measurements were made at laboratories under contract with the Atomic Energy Commission.

There are 6 tables of numerical data and 3 graphs to illustrate the leading features of the findings. The data are unsuitable for abstracting, but will prove an invaluable source of reference. *S. Russ*

NORWOOD, W. D. **DTPA—Effectiveness in removing Internally Deposited Plutonium from Humans.** *J. Occup. Med.* Chicago. 1960, Aug., v. 2, No. 8, 371–6, 1 fig. [14 refs.]

This article gives the results of treatment of 6 employees having measurable amounts of Plutonium (Pu^{239}) in their bodies, by means of injections of DTPA. This substance has proved effective in hastening the processes of elimination (urine and faeces) and readers may like to have its chemical structure:—



In other words "Trisodiumdiethylenetetraminepentaacetic acid". The material was administered intravenously by slow drip once or twice a day; 250 c.c. of isotonic saline solution contained the DTPA. The daily dose varied from 0·1 to 2·0 gm. Complete details of the tests are given in Table 1 from which may be gathered the salient results. Only in one case was there intolerance to the drug which necessitated a curtailment of treatment.

Comparisons are made of these results with those obtained by others in the use of EDTA which points to the superiority of the drug under review. These agents can show toxicity and the author is careful to point out that "this drug should not be used in the presence of nephritis and other kidney pathology and should be used only with proper evaluation of the patient's renal state before, during and after therapy." *S. Russ*

HOUGHTON, J. A. & LEE, G. **Data on Ultraviolet Absorption and Fluorescence Emission.** *Amer. Indust. Hyg. Ass. J.* 1960, June, v. 21, No. 3, 219–30, 4 figs. [37 refs.]

This article contains 2 long tables which present data from the literature concerning determinations of air contaminants, supplemented by data from the laboratory of the Liberty Mutual Insurance Company, Hopkinton, Massachusetts. In reporting UVR data, curves were drawn by plotting the logarithm of the molar absorptivity against the wavelength in millimicrons, and data presented in the literature by other methods have been converted to this basis. In reporting fluorescence data, only the major maxima have been tabulated and both the activation peaks and fluorescence peaks are given. The concentrations reported are the minimum values which are reliable. The causes of variations in reports from various sources are mentioned, and methods to achieve reliability are discussed as well as procedures for both tests. Figures illustrate curves with aniline and aniline sulphate.

By following and maintaining standardized conditions, reproducible results can be obtained with quantitative fluorescence and UVR absorbance methods. The data tabulated give the analyst a start in setting up a method for sampling and analysis. *M. Patricia Fitzsimons*

Food and Nutrition

The order in this section is:—**General; Foodstuffs; Food Poisoning.**

FOODSTUFFS

Composition and Bacteriological Control

GUINÉE, P. A. M. & KAMPELMACHER, E. H. Enkele gegevens omtrent het gebruik van ophopingsmedia bij het bacteriologische onderzoek van vlees en organen van slachtdieren. [**Some Data about the Use of Enrichment Media in Bacteriologic Inspection of Meat and Organs of Slaughter Animals**] *Tijdschr. v. Diergeneesk.* 1960, Aug. 1, v. 85, No. 15, 951–6.

The English summary appended to the paper is as follows:—

"Out of 577 samples of meat and organs, derived from slaughter cattle and bacteriologically tested according to inspection- regulation rules, 11 × *Salmonella* was isolated; from the same samples 44 × *Salmonella* was isolated by means of enrichment media. It is suggested to make the use of enrichment-medium of Müller obligatory, followed by inoculation on brilliant green phenol red agar plates with a diameter of 14 cm."

GALBRAITH, N. S., HOBBS, Betty C., SMITH, Muriel, E. & TOMLINSON, A. J. H. **Salmonellae in Desiccated Coconut. An Interim Report.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1960, June, v. 19, 99–106. [16 refs.]

Desiccated coconut from Papua was incriminated as a vehicle of infection in the typhoid outbreak that occurred in Australia in 1953 [WILSON and MACKENZIE, this *Bulletin*, 1956, v. 31, 659]. Samples from Ceylon were found to be contaminated with coliforms but not salmonellae. Nevertheless further investigations by KOVACS [*ibid.*, 1959, v. 34, 1033] showed that the Ceylon coconut was contaminated with *Salmonella paratyphi B* and other salmonellae. During all stages of processing coconut there are opportunities for contamination with intestinal Gram-negative bacteria and the material itself is an excellent culture medium for these organisms. In view of the fact that dried coconut is widely used in the manufacture of confectionary the possible hazards to health from such a product are obvious.

The Public Health Laboratory Service has recently made an extensive survey of Ceylon desiccated coconut imported into Great Britain, and from more than 850 separate samples 9% have been found to be contaminated with *Salm. paratyphi B* and other members of the group. This interim report also gives some of the results of experimental sterilization procedures which are being tried out for reducing the hazard without reducing the acceptability of the raw product as a food-stuff. Heat treatments tend to make desiccated coconut less attractive as a sweet-meat but good reports have been obtained after treatment with ethylene oxide. The results of further investigations will be awaited with interest.

H. J. Bensted

THATCHER, F. S. & ROSS, Doreen. **Multiplication of Staphylococci during Cheese Making. The Influence of Milk Storage Temperatures and of Antibiotics.** *Canadian J. Pub. Health.* 1960, June, v. 51, No. 6, 226–34.

Milk obtained from cows which had not received antibiotic treatment for several months, and also from a single cow receiving chlortetracycline therapy for incipient mastitis, a mixed lactic "starter" culture containing *Streptococcus lactis* and *Streptococcus cremoris*

and commercial rennet were used in simulated cheese manufacture.

Coagulase-positive staphylococci were counted by plating on mannitol-salt agar (Difco) incubated at 37°C. for 48 hours. It was found that the following factors in relation to milk quality contributed to the development of massive populations of staphylococci in cheese: substantial contamination with staphylococci originating from the bovine udder; inadequate overnight cooling; presence of antibiotic residues; contamination with strains of staphylococci resistant to the antibiotics present in the milk.

There was no significant multiplication of staphylococci in milk held at 10°C., but at 22°C. there was a 3-fold increase after 5 hours, and a 1,000-fold increase after 21 hours. When the milk was raised to a temperature of 35°C. before holding at room temperature there was a 30-fold increase at 5 hours and a 6,000- to 10,000-fold increase in 21 hours. The final staphylococcal population seemed proportional to initial numbers in the milk.

Levels of penicillin in the milk, at or higher than 0·01 IU per ml., reduced the rate of multiplication of the penicillin-susceptible strains. A chlortetracycline-resistant strain multiplied at an unusually rapid rate in milk containing residues of chlortetracycline.

Staphylococci increased rapidly during the period of heat treatment after coagulation of the casein. The numbers of staphylococci in the pressed curd bore a positive relationship to the numbers of staphylococci present in the milk at the start of the cheese-making process. Staphylococci in excess of 500 million per gm. had been demonstrated in the curd.

The presence of low levels of penicillin in the milk tended to decrease the rate of multiplication of staphylococci during cheese making but in the presence of penicillin at concentrations of 0·01 to 0·05 IU per ml. the lactic streptococci were repressed to a greater degree than the staphylococci so that the ratio of staphylococci to lactic streptococci ranged to 15 : 1 (in the presence of 0·03 IU penicillin). The *p*H of curd made under these various conditions showed no consistent difference from that of control preparations; it is considered that acid produced by staphylococci contributed to the characteristic *p*H change. The influence of other bacteria on the multiplication of staphylococci could be stimulatory, repressive or of no effect.

Two public health hazards are envisaged: staphylococcal food poisoning of which severe outbreaks have occurred recently, and the dissemination into the community of larger populations of virulent strains of staphylococci. *Betty C. Hobbs*

WEDDERBURN, Doreen L. **Antiseptic Cream for Use on the Hands in Food Establishments.** *Brit. J. Indust. Med.* 1960, Apr., v. 17, No. 2, 125–9, 1 fig.

Antiseptic cream containing benzalkonium chloride is recommended for use on the hands, immediately after washing with soap and water, in food factories.

Zone inhibition tests showed that the cream was active against coagulase-positive staphylococci particularly, and to a lesser extent against *Escherichia coli* and *Salmonella typhi-murium*. The inhibitory film on hands remained active against staphylococci for at least 2 hours while wet and dry work was carried out. After application to skin deliberately contaminated with large numbers of staphyloccocci it was shown that 91–95% of organisms were destroyed in 10 minutes and 98% in 30 minutes. The cream reduced the bacterial flora on hands of laboratory and office workers during a period of 2 hours in comparison with the flora of hands smeared with control cream. The results of tests in food factories indicated that *E. coli* on hands could be eliminated by using this cream.

For 1 year more than 500 people had applied the cream without adverse effect on the skin.

Betty C. Hobbs

See also p. 1164, RAMADAN, **Comparative Studies on the Detection of Pollution of Water, Milk, and Ice Cream.**

FOOD POISONING

SEELIGER, H. P. R. **Food-Borne Infections and Intoxications in Europe.** *Bull. World Health Organization.* Geneva. 1960, v. 22, No. 5, 469–84, 1 fig. [44 refs.]

Food-borne infection is restricted to "clinically apparent or inapparent infections caused predominantly by micro-organisms, or almost exclusively transmitted by directly or indirectly contaminated food", bacterial food poisoning to the recognized intoxications, *i.e.* "to bacterial food-borne diseases which are not transmitted directly from man to man, or from man to animal, and which are characterized by toxic symptoms".

The increase in food-borne disease is explained by the effect of war, the importation of food for human beings and animals from areas where hygiene is poor, and from tropical countries, the growing habit of taking at least one meal in a canteen or restaurant, and to international travel. It is recognized that the reporting of incidents varies from one country to another as does the precise method of classification of the various diseases. Statistics are given for the incidence of salmonellosis in England, France and Germany.

The great majority of food infections are attributable to salmonellae, and predominantly to *Salm. typhi-murium*, the phage typing of which is invaluable to the epidemiologist.

Apart from endemic serotypes the importation of infected animals or their contaminated products is causing outbreaks of salmonella infections, many salmonella

serotypes isolated from animal feeding stuffs, fish, bone, blood and whale meal, egg products and carcass meat, are identified with those found in human infections and animals.

Not all salmonella species found in imported food have been isolated from human or latent animal infections; it is thought that some strains of tropical salmonellae will not easily adapt themselves to hosts in non-tropical areas, while other species become adapted and settle down to infect food, cheese, milk and milk products.

Shigella infections and particularly *Shigella sonnei* are prevalent throughout Europe. Both Salmonella and Shigella strains, except *Sh. sonnei* are spread by food in a haphazard manner. The role played by other enterobacteriaceae and related organisms such as *Alkaligenes, Aeromonas* and *Pseudomonas* in food-borne infection is unknown. Bovine tuberculosis from milk and milk products, pasteurellosis, especially *Pasteurella pseudotuberculosis,* brucellosis, tularaemia from infected hare's meat, listeriosis from nonpasteurized milk, eggs and meat, and *Erysepilothrix rhusiopathiae* from animal products are also mentioned under food-borne infection.

Food-borne intoxication occurs after the formation of toxin in food during storage. The prevention of staphylococcal enterotoxin food poisoning is concerned with culinary techniques and rapid refrigeration. The phage typing of staphylococci is essential for epidemiological investigation.

Of the sporing bacilli, *Clostridium botulinum* rarely causes trouble in the western and central parts of Europe at the present time, although small outbreaks due to type B have occurred fairly recently in Norway and Germany, while type E outbreaks have occurred in Denmark. Heat-resistant *Cl. welchii* is important in England, France, Germany and Norway; the common vehicles are meat and sauces prepared on a large scale and kept at a temperature favourable for bacterial growth.

Bacillus cereus food poisoning has been described in Norway, Denmark, Sweden, The Netherlands, and Hungary; large numbers of the organism must be present in the food before ingestion; the aetiology of the disease is a matter for discussion.

Control of food-borne infection depends on collaboration between public health and veterinary public health authorities. *Betty C. Hobbs*

HART, C. J., SHERWOOD, W. W. & WILSON, Elizabeth. **A Food Poisoning Outbreak aboard a Common Carrier.** *Pub. Health Rep.* Wash. 1960, June, v. 75, No. 6, 527–31.

In the spring of 1959 nearly 50% of 450 passengers on a special train were taken ill with gastro-enteritis; 25 required hospitalization. This outbreak is recorded as one of the largest in the U.S.A. Symptoms consisted primarily of severe abdominal cramps and watery diarrhoea with nausea and vomiting less prominent, pyrexia was recorded in two cases only. The duration of illness was approximately 12 hours, the incubation period recorded for 181 patients ranged from ½ to 26½ hours, with a mean of 9 hours, 35 minutes.

The suspected dinner consisted of roast turkey, dressing, gravy, cranberry sauce, mashed potatoes, green peas, bread, butter, ice-cream sundae, coffee, tea or milk. Of these the turkey and turkey dressing were suspected as the vehicles.

Preparation of the turkeys had started the day before the meal; some parts were boiled to make the stock for dressing and gravy, others were baked, all were cooled for 2 hours before storage overnight in a "wet ice" box at 62°C. Similar preparations were carried out on the day of the meal, when the stock was not refrigerated. The turkey was sliced cold during the afternoon, reheated in stock in the oven for about 45 minutes and kept warm on the top of the stove.

All samples of food were negative for salmonellae and coagulase-positive staphylococci, but the cooked turkey and turkey dressing contained large numbers of bacteria. One sample of turkey had a count of 43 million per gm. of which the most probable number (MPN) of enterococci was 4·6 million per gm. A sample of turkey dressing showed a plate count of 37 million per gm. with the MPN for enterococci of 240 million per gm.

Samples of uncooked frozen turkey gave plate counts of $8-72\times10^3$ per gm. and the MPN of enterococci was less than 100 per gm. It seemed, therefore, that there had been heavy bacterial growth in the food after preparation.

Organisms resembling *Clostridium welchii* were isolated from thioglycolate enrichment cultures of turkey dressing, and also from 13 of 25 rectal swabs from hospital patients. The strains of clostridia were not typical of those causing food poisoning in England and they were not serologically identical.

Although diarrhoea and cramps are prominent in both enterococcal and clostridial food poisoning, the occurrence of vomiting in 24% of patients in the present outbreak resembles reported enterococcal outbreaks more nearly than clostridial [this *Bulletin,* 1953, v. 28, 649; 1956, v. 31, 659].

It is concluded that there was a need for greater care in the handling of food served to the public, for adequate facilities and for additional training and supervision of employees.

It is pointed out that enterococci and *Cl. welchii* should be considered as possible causative organisms in food poisoning. Laboratories should be equipped for the identification of these organisms which may be responsible for outbreaks of undetermined aetiology, which now account for about one half of the approximately 200 outbreaks reported annually in the United States.

Betty C. Hobbs

FEY, H. & WIESMANN, E. Die Gefahr des Salmonellenimportes mit Eiprodukten und tierischen Futtermitteln. **[The Danger of Introduction of Salmonella Infection with Preparations of Egg and Specialized Animal Fodders]** *Schweiz. med. Woch.* 1960, July 23, v. 90, No. 30, 791–3. [23 refs.]

A family outbreak of food-poisoning in which *Salmonella enteritidis* and later Salm. Blockley were isolated from the householder, Salm. Schwarzengrund

from his wife and Salm. Blockley from the domestic servants is described.

Investigation of the confectioner's establishment from which their cakes were bought revealed that a dried egg product imported from the U.S.A. was in use and yielded 5 different salmonellae: Schwarzengrund, Blockley, *anatum*, Chester and Give. This observation is made the ground for a comprehensive survey of the literature of many countries dealing with the dangers of salmonella infection due to importation of egg-powders, fish-meals, cattle-fattening products and products designed to accelerate egg-production by poultry.

There is ample evidence that in Switzerland as elsewhere the number of salmonella infections is steadily mounting and that among these many forms previously peculiar to the countries from which the imported products emanated are being observed. The products from Angola and from China appear to be particularly dangerous. Methods of control and the extent to which they can be effective are discussed. *J. W. McLeod*

Mycoses and Mycology

The order of diseases and fungi in this section is:—**General; Dermatophytes; Blastomyces; Histoplasma, Sporotrichum, Phialophora; Candida, Cryptococcus; Actinomyces, Nocardia; Aspergillus; Others.**

Papers on Blastomycosis (South American type), Coccidioidomycosis, Mycetoma and Rhinosporidiosis are abstracted in the TROPICAL DISEASES BULLETIN.

MARTIN, W. J. & NICHOLS, D. R. **The Mycoses.** *Proc. Staff Meetings Mayo Clinic.* 1960, Mar. 30, v. 35, No. 7, 149–61. [23 refs.]

This is an excellent up-to-date summary of the chief clinical features of the systemic mycoses as they occur in man and includes useful notes on laboratory findings and treatment.

In concluding paragraphs the authors discuss the merits and use of amphotericin B in the treatment of a number of these mycoses. *C. J. La Touche*

BALABANOFF, V. A. Antibiose und Dermatophyten. [**Antibiosis and Dermatophytes**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 179, No. 2, 241–54, 10 figs. [34 refs.]

This paper from the Dermatology Clinic of the Faculty of Medicine at Sofia reports the cultivation from mycotic skin lesions of mixtures with the causative fungus of other micro-organisms exhibiting antagonism to it. A "glass bead" method of demonstrating this is described, which consists of growing the antagonistic organism on medium in a Petri dish, placing 8–10 hot glass beads on the surface, detaching the medium with a spatula, inverting it, and inoculating the under surface with the other organism. The illustrations do not show this method but only the effects of contiguous growth on the same surface: this was sometimes stimulatory rather than antagonistic, one organism growing out towards the other or accentuating pigment formation by it. Apparently some organisms exerting an antagonistic effect were fungi and other bacteria: among the latter *Bact. faecalis alkaligenes* is alone in being named.

[This paper is difficult to follow, and not wholly convincing. Some of the illustrations purporting to show antagonism do not seem to indicate it very clearly, and Fig. 6, showing inhibition of *Trychophyton gypseum* by *Bact. faecalis alkaligenes* could be explained in 2 very ordinary ways: by the bacterium growing faster and thus occupying space first, or by its raising the *p*H of the medium and thus rendering it uncongenial to the fungus.] *L. P. Garrod*

HARVEY, G., ALEXANDER, J. O'D. & KIRK, J. F. **Griseofulvin in Fungous Infections.** *Scottish Med. J.* Glasgow. 1960, Feb., v. 5, No. 2, 51–6, 1 coloured fig.

The authors of this article record the results of treatment of 51 cases of dermatophytosis with oral griseofulvin. The patients were distributed as follows according to the clinical type of lesion with which they presented: 20 patients (ringworm of nails said to be due to *Trichophyton rubrum*); 21 patients (foot infection said to be due to *Epidermophyton floccosum*); 7 patients (pustular ringworm due to unspecified fungi) and 3 (ringworm of scalp due to *Microsporum canis*).

The authors claim a high proportion of cures among these patients except in the case of nail infections which take longer to clear than infections of the smooth skin and scalp: however, 8 of these were cured and 9 improved. Allergic (epidermophytid) reactions disappeared rapidly as a result of treatment.

Toxic reactions to the drug were negligible.

The authors advise supplementary topical treatment, including such measures to prevent reinfection as: paring of diseased nails, shaving of affected areas of the scalp, and the application of keratolytic ointment to skin lesions.

The usual dose of griseofulvin was 1 gm. daily for adults and 0·5 gm. for children, given in tablets each containing 250 mgm. Duration of treatment varied from 2 to 29 weeks. The patients were followed up over a period of 8 months. *C. J. La Touche*

La Touche, C. J. **Mouse Favus due to *Trichophyton quinckeanum* (Zopf) MacLeod & Muende: a Reappraisal in the Light of Recent Investigations. IV.** *Mycopathologia.* The Hague. 1960, June 30, v. 13, No. 1, 33–47, 1 text fig. & 19 figs. on 4 pls. [14 refs.]

Continuing his study [this *Bulletin*, 1960, v. 35, 1098] the author reviews in detail the cultural features of *Trichophyton quinckeanum* on Sabouraud's media and concludes that, although the macroscopic features are characteristic, on the basis of its microscopical features this dermatophyte should be assimilated with the *T. mentagrophytes* group. *G. C. Ainsworth*

Biguet, J., Cochet, G., Deblock, S., Andrieu, S. & Duc, G. Les affinités taxonomiques de quelques *Trichophyton* africains, agents de tondantes microsporiques ou trichophytiques. [**Taxonomic Relationships of Some African Forms of *Trichophyton***] *Ann. Parasit. Humaine et Comparée.* 1960, Apr.–June, v. 35, No. 3, 409–25, 12 figs. [39 refs.]

Arutyunova, S. S. & Bazyka, A. P. [**Universal Chronic Deep Trichophytosis**] *Vestnik Dermat. i Venerol.* Moscow. 1959, v. 33, No. 3, 27–30, 2 figs. [In Russian.]

The English summary appended to the paper is as follows:—

"The article describes a 60-year-old patient who for 34 years suffered from disseminated superficial chronic trichophytosis caused by Trichophyton violaceum. In 1954 following X-ray irradiation of the scalp, beard, mustache, eyebrows, armpits and pubis, with subsequent external treatment, the patient developed suppurative nodes and prominences which formed chronic indolent ulcers. Repeated treatment in clinical conditions was of no avail. A conjecture is set forth that the deterioration of the superficial process into deep trichophytosis may have been provoked by indulgence in alcohol and prolonged X-ray irradiation of large areas of the skin, leading to changes of the immuno-biological state of the body."

Ajello, L., Briceño-Maaz, T., Campins, H. & Moore, Jane C. **Isolation of *Histoplasma capsulatum* from an Oil Bird (*Steatornis caripensis*) Cave in Venezuela.** *Mycopathologia.* The Hague. 1960, Mar. 31, v. 12, No. 3, 199–206, 2 figs. [34 refs.]

Acting on previous reports of histoplasmosis in visitors to a cave near a village called Tingo Maria in Peru which was inhabited by a breeding colony of oil birds (*Steatornis caripensis*) [this *Bulletin*, 1956, v. 31, 815] the authors decided to investigate soil samples from a large cave in Venezuela which, likewise, was inhabited by oil birds.

Soil samples from this cave were, accordingly, investigated for fungi which produce systemic disease by the method of injecting mice intraperitoneally with suspensions of the soil and then at a later date examining the mice for lesions after killing them.

Histoplasma capsulatum was isolated by the authors from 2 of 15 samples obtained from this cave, thus tending to confirm that the oil bird was in some way responsible for its presence in the soil in such sites, although this organism has also been isolated from caves in which bats were established [*ibid.*, 1959, v. 34, 224]. In this cave bats were not found. *C. J. La Touche*

Gellert, A. **A Case of Histoplasmosis successfully treated with Amphotericin B.** *East African Med. J.* 1960, July, v. 37, No. 7, 501–7.

Howard, D. H. **Effect of Mycostatin and Fungizone on the Growth of *Histoplasma capsulatum* in tissue culture.** *J. Bacteriology.* 1960, Mar., v. 79, No. 3, 442–9, 1 fig. [25 refs.]

In tissue culture experiments [this *Bulletin*, 1960, v. 35, 32] in which mouse peritoneal exudates were parasitized with *Histoplasma capsulatum* yeast phase cells, the inhibitory effect of nystatin [Mycostatin] and amphotericin B [Fungizone] on this organism was investigated.

It was found that concentrations of nystatin at the level of 250 units per ml. were toxic to the macrophages in the peritoneal exudates but that concentrations of 100 units per ml. or less were relatively non-toxic. Amphotericin B was toxic at a concentration level of 10 μgm. per ml., "partially toxic at 5 μg. to 0·5 μg./ml. and relatively non-toxic at 0·1 to 0·5 μg/ml."

The addition of 25 units of nystatin or 0·1 μgm. of amphotericin B completely depressed the destructive effects of *H. capsulatum* on cell cultures.

These drugs markedly reduced the number of macrophages parasitized by *H. capsulatum* and altered the staining properties of yeast phase cells in the macrophages, showing that they were able to exert their effect on these parasites within the cells as well as outside the cells.

It was also shown that minimum concentrations which could inhibit extracellular multiplication of the parasite were also able to affect parasites situated within the macrophages. *C. J. La Touche*

Londoño, F. Apuntes sobre esporotricosis. A proposito de un caso tratado con anfotericin B. [**Observations on Sporotrichosis. A Case Treated with Amphotericin B**] *Rev. Facul. de Med.* Bogotá. 1960, Jan.–Mar., v. 28, Nos. 1/3, 23–7, 2 figs. [14 refs.]

The English summary appended to the paper is as follows:—

"1. A brief historical review is incorporated of the early literature on Sporotrichosis.

"2. The fact that Sporotrichosis is widely disseminated in Columbia is emphasized.

"3. The lack of bibliographical data is noted on extra-cutaneous forms of Sporotrichosis.

"4. The intracutaneous reaction with 'Esporotriquina' is of great assistance in arriving at a diagnosis of this disease.

"5. A case is reported of Verrucose Sporotrichosis treated with Amphotericin B with excellent results."

KUTSCHER, A. H., SEGUIN, Lucile, ZEGARELLI, E. V., RANKOW, R. M., CAMPBELL, J. B. & MERCADANTE, J., with the assistance of H. PEARSON. **Pagano-Levin Culture Medium for Differentiation of *Candida albicans*. American Type Culture Collection Studies. 1.** *Antibiotics & Chemotherapy*. New York. 1959, Nov., v. 9, No. 11, 649–59, 1 fig.

"According to Pagano *et al.*, the differentiating quality of the medium depends on the differing abilities of various yeasts and fungi to reduce a tetrazolium compound included in the medium to insoluble, coloured formizans; *C. albicans* does so either not at all or to a very limited extent." (*Antibiotics Annual, 1957–58*, New York 1958, p. 137.)

The authors record in this paper data resulting from their application of this differential technique to a mixed group of 94 yeasts and other fungi. These included 22 strains of *C. albicans* and 39 strains of other species of *Candida*.

As the differential technique is based partly on the colour shade which given colonies assume on Pagano-Levin culture medium, a colour standard chart is provided for use in determining more accurately the shades observed. The critical component shades on this chart are based on mathematical formulae and each shade has a symbol, *e.g.* R4.

Colonies of *C. albicans* assume a creamy or faintly pink colour not in excess of R4 on the standard colour chart. Two other criteria besides colour, namely creamy texture and moistness, are required to characterize *C. albicans* strains on this medium.

The authors found that it was necessary to wait 4 days before all 3 criteria could be realized and before colonies could be reported as belonging to the species *C. albicans*. They also found that after 6 days' growth the colour of *C. albicans* colonies became darker, so that colour, at this stage, could no longer be relied upon as a criterion of identification. Moreover, it is suggested by them that cultures of *C. albicans* which have satisfied these 3 criteria on Pagano-Levin medium should subsequently be sub-cultured to media appropriate for the production and observation of chlamydospores in order to confirm morphologically the results obtained in Pagano-Levin medium. *C. J. La Touche*

WINNER, H. I. **Experimental Moniliasis in the Guinea-Pig.** *J. Path. & Bact.* 1960, Apr., v. 79, No. 2, 420–23, 8 figs. on 2 pls. [11 refs.]

The author reports in this article the results of his studies of the pathogenicity of a strain of *Candida albicans* which he injected into guineapigs by several routes, *viz.* intradermal, intraperitoneal and intravenous.

Intradermal injection produced a localized abscess which became ulcerated and in due course extruded its content, leaving a clean ulcer which soon healed. The evolution of this lesion lasted about 2 weeks.

Intraperitoneal injection resulted in limited spread of the infective process which was confined mainly to the peritoneal surfaces, and in some cases to the peripheral part of the liver.

Intravenous injection with various concentrations of yeast cells showed that, for this strain of *C. albicans*, the severity and extent of the distribution of the lesions in the guineapig were dependent on the concentration of the inoculum, the apparent threshold dose for producing fatal infection being in the neighbourhood of 80,000 organisms per gm. body weight.

Although few yeast cells were found in the lungs in necropsy material, the most prominent lesions were pulmonary congestion and oedema, and these appeared to be the immediate cause of death.

Other viscera affected were: the brain, the heart, the liver and the kidneys, and *C. albicans* was found in all of them in the form of yeast cells and mycelium in varying quantity.

Attempts to assess the value of cortisone when administered in association with these experimental inoculations showed that this drug had no apparent influence on the course or severity of the resultant infection.

C. J. La Touche

QUINN, L. Y., WILBUR, R. D. & CATRON, D. V. *In vitro* **Response of *Candida albicans* and *Candida tropicalis* to Antifungal Agents.** *Antibiotics & Chemotherapy*. New York. 1960, Feb., v. 10, No. 2, 95–100. [12 refs.]

In view of an observed association of *Candida tropicalis* with stools obtained from pigs suffering from "scouring" as a result of being fed on diets containing antibiotics, the authors of this article set themselves the task of assessing the effect of various antifungal agents on this organism and on *C. albicans* under conditions approaching those encountered in practice.

The strain of *C. tropicalis* used in these investigations was obtained from scouring pigs, and *C. albicans* strains were obtained from the American Type Culture Collection.

The culture medium, which was a water clear preparation, included a large number of ingredients which were said to be incorporated in the pigs' diet.

The drugs tested were nystatin, A–5283 [also shown in the text as A–5293], Amphotericin B, chlortetracycline and 3-nitro-4-hydroxyphenylarsonic acid (3 N4HPAA).

Results showed that nystatin, A–5283 (Lederle) and Amphotericin B were active against these 2 yeast species at a concentration of 10 μgm. per ml. and that the activity of both nystatin and A–5283 decreased with decreasing concentration of these drugs. In contradistinction, amphotericin B was as effective at 2·5 μgm. per ml. as it was at 10 μgm. per ml. Finally, no stimulating effect on either *C. albicans* or *C. tropicalis* was noted when chlortetracycline was added to the medium.

C. J. La Touche

ČERNÍK, L., HÔTÂN-PHI, DOAN HÔNG-HOA, ŠERÝ, V. & PHAM VÂN-NÔNG. Syndrom tzv. velké alimentární anafylaxe při přecitlivělosti na *Candida tropicalis*. [**Syndrome of So-Called Major Alimentary Anaphylaxis in Hypersensitivity to** *Candida tropicalis*] *Časopis Lékařů Českých*. Prague. 1960, Aug. 12, v. 99, Nos. 32/33, 1023–8. [20 refs.]

The English summary appended to the paper is as follows:—

"The authors present a report (from the Czechoslovak hospital in Hai-phong, Vietnam People's Republic) on the seasonal mass incidence of the syndrome of so-called major alimentary anaphylaxis, caused by the consumption of pine-apples contaminated with Candida tropicalis. The affected persons (12 Vietnamese) were mostly allergic individuals with professions predisposing to allergy to moulds and fungi. The authors assume as a result of the examinations made, that the pine-apple only mediated the massive contact with the specific allergens, and they also draw attention to the significance of fungi and moulds as causal agents on bronchial asthma and chronic asthmoid bronchitis in the Vietnam People's Republic.

"The opportunity to investigate this uncommon type of mould allergy in a large number of patients provided some data on the causes and the prevention of the syndrome of so-called major alimentary anaphylaxis."

FITZPATRICK, M. J. & POSER, C. M. **The Management of Cryptococcal Meningitis.** *Arch. Intern. Med.* 1960, Aug., v. 106, No. 2, 261–70, 6 figs. [26 refs.]

"Our experience in management of six patients with cryptococcal meningitis in the past four years is presented. In four patients, amphotericin B therapy was used. In three, the drug was used in intravenous treatment, and all survived. The role of excisional surgery and chemotherapy in management of cryptococcosis is discussed."

BARRASH, M. J. & FORT, M. **Amphotericin B Therapy in Torula Meningitis.** *Arch. Intern. Med.* 1960, Aug., v. 106, No. 2, 271–4.

"A case of torula meningitis responding rapidly to amphotericin B is presented. Some observations concerning details of treatment with this agent are also presented, and an alert is sounded as to a possible toxic effect on the blood-forming organs. Amphotericin B is the drug of choice in torula meningitis and may prove to be curative in some cases."

RIOPEDRE, R. N., DE CÉSARE, I., MIATELLO, E., CARÍA, M. A. & ZAPATER, R. C. Aislamiento de *Rhodotorula mucilaginosa* del L.C.R., heces, orina, exudado faríngeo y piel de un lactante de 3 meses. [**Isolation of** *Rhodotorula mucilaginosa* **from the Cerebrospinal Fluid, Faeces, Urine, Pharyngeal Exudate and Skin of an Infant aged 3 months**] *Rev. Asoc. Med. Argentina.* 1960, July, v. 74, No. 7, 431–4, 1 fig.

The English summary appended to the paper is as follows:—

"A three month-old infant was admitted to hospital with signs and symptoms of meningoencephalic irritation. From the CSF, pharyngeal smear, faeces, urine and skin, a yeast was isolated which proved to be Rhodotorula mucilaginosa.

"Inoculation of the different cultures to mice caused their death in cachexia. The same yeast was isolated from lesions in the liver and spleen of the mice.

"The patient improved without specific treatment and became cured without sequel. This case is believed to be the first one reported in the pediatric literature."

RAINS, A. J. H., BARSON, G. J., CRAWFORD, N. & SHREWSBURY, J. F. D. **A Chemical and Bacteriological Study of Gallstones. The Presence of an Actinomycete.** *Lancet.* 1960, Sept. 17, 614–18, 2 figs. [19 refs.]

GRCEVIC, N. & MATTHEWS, W. F. **Pathologic Changes in Acute Disseminated Aspergillosis. Particularly Involvement of the Central Nervous System.** *Amer. J. Clin. Path.* 1959, Dec., v. 32, No. 6, 536–51, 20 figs. [54 refs.]

These authors describe 3 fatal cases of disseminated aspergillosis involving, amongst other organs, the brain.

The first case was of a 36-year-old white male farmer admitted to hospital in a semi-comatose state. The second case was of a 13-year-old white boy who, on admission, was severely jaundiced and was suffering from protracted epistaxis. The third was of a 22-year-old white foundry moulder who was admitted to hospital in a comatose state.

While the case reports of these patients differed in detail, they revealed a common general pattern. Thus, all 3 were suffering from some severely debilitating disease; were comatose on admission, or shortly afterwards; were treated with antibiotics (and in one case also with steroids); and soon afterwards all rapidly deteriorated to a fatal termination. Moreover, in all 3, histological investigations of autopsy material showed numerous lesions in the brain, lungs and myocardium with which mycelium of *Aspergillus* type was associated. Of special interest was the tendency of this mycelium to invade blood vessels, a tendency also shown very prominently by mycelium of species of the Mucorales in cases of mucormycosis [this *Bulletin*, 1960, v. 35, 875].

C. J. La Touche

Communicable Diseases

The order in this section is:—**Tuberculosis; Venereal Diseases; General Infective Diseases; Other Communicable Diseases.**

For the bacteriology of these diseases see the section on Bacteriology below. For diseases conventionally regarded as tropical, readers are referred to the TROPICAL DISEASES BULLETIN.

TUBERCULOSIS

VAN ZWANENBERG, D. **Experience in Tracing Sources of Infection of Tuberculin Converters.** *Tubercle.* 1960, June, v. 41, No. 3, 171–7. [13 refs.]

A tuberculin index was established in Ipswich, England [population 105,000] in which the results of tuberculin testing of children were recorded. The register contained the results of some 20,000 tests at the time of writing, which means that slightly less than half the children in the area had been tested at least once in the previous 3–4 years. Schoolchildren were tested at each of their 3 routine medical inspections, all children referred to the chest clinic were tested also as were all contacts of known or suspected cases of tuberculosis and some children in certain hospital wards. The Heaf test has been used since 1953.

Up to July 1958, 109 tuberculin converters had been discovered through the index, and in 95 of these the cause of conversion was investigated as far as possible. A probable source of infection was found for 31. 28 of the 31 were probably infected by 23 individuals of whom 16 were already known to the tuberculosis service and 7 were newly discovered. Milk was thought to be the source of infection of 3 children.

The discovery of the source of infection in less than one-third of the cases is disappointing. More sources of infection were found when the interval between negative and positive tests was less than a year, all the children in the household converted, and the child developed a manifest tuberculous lesion. There were 6 children with definite lesions in the "explained" group and only 1 in the "unexplained" group. Where all the children in a family converted a probable source of infection was found in 75%.

It is concluded that this technique by itself is at present insufficient to control tuberculosis in a community where there is a large population and communications are free and extensive. *H. G. Calwell*

PANÀ, C., RUSTICHELLI, V. & FINOCCHI, F. Indagini tubercoliniche e schermografiche in un gruppo di ultrasessantenni. [**Tuberculin Reactions and X-rays Examinations in a Group of Persons over 60 Years Old**] *Lotta c. la Tubercolosi.* 1960, May–June, v. 30, Nos. 5/6, 369–80, 1 fig. [25 refs.]

After pointing out the present-day importance of pulmonary tuberculosis in people over 60 years old, the authors mention that they carried out in May–June 1959 an investigation under the auspices of the Rome Provincial Anti-Tuberculosis Society into the incidence of tuberculosis in persons over 60. All the people examined were ambulant but were in geriatric wards of various institutions in Rome [and hence were a selected population]. Each was Mantoux-tested by 0·1 cc. PPD (= 1 unit or 0·1 cc. OT 1/10,000) and immediately after had a miniature film taken by a mobile unit; the Mantoux was read 48 hours later. All those whose small film showed pleuropulmonary lesions were examined by full-sized films and tomography. In all, 369 males and 647 females were tested, the numbers by age-groups being as follows: 60–69, 237; 70–79, 484; 80+, 259.

655 were found to be Mantoux positive. 101 who were Mantoux negative showed suggestive lesions in the films indicative of past tuberculosis. Thus practically 75% were positive, a percentage which, the authors consider, is still below the true figure, which they put at 80%. The miniature films showed 391 persons to have suggestive present or past lesions, 25% of whom were Mantoux negative.

The results of the 2 tests were compared. Among the Mantoux positive subjects there was no active case in the 60–69 age-group; there were 3 in the 70–79 age-group; and 3 in the 80+ group. The figures for inactive tuberculosis were 1 in the 60–69 group; 4 in the 70–79 group; and 2 in the 80+ group. 77 subjects in the 60–69 group, 125 in the 70–79 group, and 75 in the 80+ group showed healed lesions. Persons in the Mantoux-negative groups showed neither active nor inactive disease, but healed lesions in 101 cases.

The authors point out particularly that a fall in resistance due to advancing years can cause inactive tuberculosis to assume a very active exudative form which it is almost impossible to arrest, hence the importance of its detection. No pulmonary tuberculomas were found but 7 fibronodular forms were seen among the inactive cases. A definite cavitating lesion of the right apex was found in an 81-year-old man and a miliary infection of both upper lobes in a 73-year-old person.

The authors consider that the percentage of Mantoux positives remains practically stationary in people over 60 but women in the 70–79 group were less often affected with actual disease than those in the 2 other age-groups or any of the men. They emphasize that before ascertaining the figures given, all persons with pleuropulmonary lesions which were not clearly tuberculous in origin were excluded, and they stress the danger of the lesions found as the organisms were still very active biologically. Finally they point out that, as has already been stated by DADDI, the Mantoux test is the simplest and best method of detecting infected and infective persons in the age-groups over 60.

[This paper, of which the authors themselves say that they have not been able to find anything exactly comparable, deserves to be read in full.]

W. K. Dunscombe

CROFTON, J. **Drug Treatment of Tuberculosis. I. Standard Chemotherapy.** *Brit. Med. J.* 1960, July 30, 370–73. **II. Treatment of Patients with Tubercle Bacilli resistant to Standard Chemotherapy.** *Ibid.*, Aug. 6, 449–51.

In these articles Professor Crofton gives an excellent summary of the present methods of treatment of pulmonary tuberculosis by drugs as carried out in Edinburgh. In the first article he gives a résumé of the toxic effects of the standard drugs followed by the recommended drug combinations. In hospital patients under the age of 40 he recommends streptomycin 1 gm. daily intramuscularly, with sodium PAS, 5 gm. three times daily, and isoniazid 100 mgm. twice daily. For hospital patients over 40 he reduces the dose of streptomycin to 1 gm. 3 times weekly because of the risk of vestibular disturbance. In mild cases treated as out-patients, and after discharge from hospital he gives 5 gm. of sodium PAS together with 100 mgm. of isoniazid both twice daily in the same cachet. He recommends that in severe cases the treatment should not be less than 2 years, but thinks that there is little evidence that a duration of more than 2 years is necessary.

In the second article he deals with the treatment of patients with tubercle bacilli resistant to standard chemotherapy. A short résumé is given of the various drugs available: pyrazinamide, 1314 (ethionamide), viomycin, and cycloserine. The article then gives an account of how patients with tubercle bacilli resistant to the standard drugs in various combinations should be treated.

Both articles give a vast amount of information in a condensed form and it is therefore impossible to abstract it satisfactorily. It should be read *in extenso* by all those interested in the treatment of pulmonary tuberculosis.

F. H. Young

TUBERCULOSIS SOCIETY OF SCOTLAND. **The Treatment of Pulmonary Tuberculosis at Work: a Controlled Trial. Report from the Research Committee** [CLAYSON, C., Chairman]. *Tubercle.* 1960, June, v. 41, No. 3, 161–70, 3 figs. [18 refs.]

This paper deals with 2 comparable groups of patients, 1 treated with antituberculous drugs and bed-rest for a period of 3 months, and the other treated with the same drugs who were allowed to remain at work. Any patient with newly diagnosed pulmonary tuberculosis could be admitted to the trial if the clinician thought it would be justifiable to treat him at work—provided that if sputum were present it was negative on direct smear or on concentration and there was no cavity with diameter greater than 2 cm. Certain types of case were excluded: patients under 15 years of age; non-Europeans; pregnant women; diabetics; patients who had had previous chemotherapy and those with collapse therapy. After sundry deductions, the numbers remaining for analysis consisted of 49 patients in the bed-rest group, and 54 patients of the group at work. 60% of the bed-rest patients were treated in hospital and 40% at home. Great care was taken that the patients in each group were comparable.

At the end of the first 3, and the end of the first 6 months the group at work remained at least as well as the bed-rest group. At 6 subsequent observation periods up to the end of 2 years progress is very similar in each group. At the end of 2 years there were 2 cases of radiographic deterioration in the bed-rest group and 4 in the group at work. In 5 of these 6 cases there was definite history that the patient had failed to take chemotherapy as requested. Details of these are given.

Reference is made to other reports of investigations of this kind [this *Bulletin*, 1958, v. 33, 25, 218] but all seem to fail in some respect to be completely convincing The propriety of treating potentially disease at work is discussed in the interim report of this investigation. Although it is clear that after 2 months' observation the patients treated at work had done as well as those who had bed rest the treatment of pulmonary tuberculosis at work is not to be undertaken lightly. It must be confined to the highly co-operative patient, and if the patient proves unreliable he should be admitted to hospital in order to ensure his compliance with the full chemotherapy regime on which his future depends. This well conducted trial is of very great interest to those who have to treat patients with pulmonary tuberculosis.

F. H. Young

CHEUNG, O. T. **Treatment of Pulmonary Tuberculosis in Diabetic Patients.** *Canadian Med. Ass. J.* 1960, July 16, v. 83, No. 3, 118–20.

This report summarizes experience in the treatment of patients who have suffered from pulmonary tuberculosis and diabetes mellitus. 27 were far advanced, 16 moderately advanced, and 7 had minimal tuberculosis. The regime was streptomycin 1 gm. twice weekly, PAS 14 gm. daily, and isoniazid 300 mgm. daily. The drugs were given throughout the patients' stay in hospital, and after discharge for a total period of 12–24 months or in some cases indefinitely. 5 patients did not receive isoniazid, as it had not been introduced at the time their treatment was started. The length of hospital and drug treatment are detailed in a table.

After treatment 35 patients had no cavity and a negative sputum and a stable radiograph; 9 patients had no cavity, negative sputum, and still clearing radiograph; 2 patients had no cavity, stable radiograph but sputum positive, and in 4 patients cavities were still present. Thus 44 patients, or 88%, had a satisfactory result from treatment. Sputum conversion occurred in 93% of patients.

As regards the diabetes, 3 patients had good control with insulin, 11 fair, and 3 poor; insulin was not required in 6 patients.

The authors conclude that the results compare favourably with those of non-diabetic tuberculous patients.

F. H. Young

GILLIS, S. **Some Aspects of Drug Resistance in Tuberculosis and its Treatment.** *Med. J. Australia.* 1960, June 25, v. 1, No. 26, 1014–19. [34 refs.]

This paper commences with a short review of the figures that have been published about the incidence of primary resistance to the antituberculous drugs in the United States and elsewhere. At the Morris Hospital, Adelaide, 440 patients were admitted bttween March 1956 and June 1959. Of these, 48 had infections completely resistant to one or more of the 3 standard drugs. On the other hand, in only 7 cases of primary resistance was the infection resistant to 2 or more drugs, as opposed to 18 cases of secondary resistance. Primary resistance was mainly to streptomycin, secondary resistance to isoniazid and streptomycin. Cases with secondary resistance were more likely to have a bad prognosis than those with primary.

Pointing out that strains resistant to streptomycin or PAS have unchanged virulence, the author notes that as far as isoniazid is concerned, this is not necessarily the case. There are 2 types of isoniazid-resistant tubercle bacilli differentiated by their ability to synthesize an enzyme-catalase, which decomposes hydrogen peroxide. Catalase-negative mutants have often a diminution of pathogenicity. Apparently isoniazid-resistant bacilli which are catalase-negative may still cause progressive human infection because of the presence at the same time of a small number of virulent sensitive bacilli.

Blood levels of isoniazid produced by a standard dose vary because of metabolic inactivation. So-called rapid isoniazid inactivators have a serum level of 0·2 μgm. or less 6 hours after the test dose, whereas slow inactivators have a level of 0·8 μgm. or more. Hence it is thought that it is advisable to estimate the isoniazid blood levels when facilities are available, so that the dose can be adjusted to reach the best therapeutic effect with the least toxicity. The effect of the alternative antituberculous drugs is then discussed. *F. H. Young*

HEYWORTH, F. & HELM, W. H. **A Comparison of the Toxic and Allergic Reactions occurring with Streptomycin and Streptoduocin in the Treatment of Pulmonary Tuberculosis.** *Postgraduate Med. J.* 1960, Aug., v. 36, No. 418, 516–18.

This compares the toxic effects produced by the use of streptomycin with those following the administration of streptoduocin. All patients who entered the Marsden Hospital at Burnley were treated with streptomycin sulphate during the first year, and those admitted during the second year were treated with streptoduocin.

All patients who completed 3 months' treatment with either preparation or in whom treatment had to be stopped because of a reaction were included in the series.

There were 100 patients treated by streptomycin sulphate, and 101 by streptoduocin. The total number of patients having a reaction who were treated by streptomycin sulphate was 40, and treated by streptoduocin was 49, but the total number of reactions was 61 with streptomycin sulphate, and 59 with streptoduocin. The type of reactions to both drugs are detailed. Among these, 20 reactions occurred with the streptomycin sulphate leading to dizziness, and with the streptoduocin only 12 patients had dizziness. On the other hand, deafness occurred in 2 with the streptomycin sulphate and 4 with the streptoduocin. 30 neurotoxic reactions occurred in 148 patients under the age of 50—an instance of 1 reaction in 5 patients—whereas in those over 50, 19 reactions occurred in 53 patients, an instance of rather more than 1 reaction in every 3 patients treated. There was no clear advantage to either preparation in the total instance of neurotoxicity or in the over-50 age-group.

Treatment had to be terminated in 14 patients in the streptomycin group, and 12 of the streptoduocin group. The authors find that in the total incidence of eighth nerve toxic effects there was no definite advantage to either streptomycin preparation in the age-group under or over 50 years. The onset of reactions was on the average slightly later with the streptoduocin (14·2 weeks) than with the streptomycin (11·8 weeks) and, therefore, longer periods of uninterrupted treatment have often been possible with the former. They conclude that, although the advantages were slight, streptoduocin was probably the drug of choice. *F. H. Young*

GILLIS, S. & TEXLER, K. **Unusual Reactions to Anti-Tuberculous Chemotherapy.** *Med. J. Australia.* 1960, July 16, v. 2, No. 3, 99–101. [10 refs.]

"Two unusual reactions to antituberculosis drugs are described, one of cholangiolitic hepatitis due to INAH, the other of hyperuricaemia due to pyrazinamide manifested solely by renal symptoms."

DEUSCHLE, K. W., JORDAHL, C. & HOBBY, Gladys L. **Clinical Usefulness of Riboflavin-Tagged Isoniazid for Self-Medication in Tuberculous Patients.** *Amer. Rev. Respiratory Dis.* 1960, July, v. 82, No. 1, 1–10, 7 figs.

"Riboflavin has been incorporated into isoniazid tablets designed for antituberculous therapy in a proportion of 50:8 by weight. Measurement of the concentrations of riboflavin in the urine of normal patients, of patients ingesting supplementary vitamin preparations, and in the urine of patients taking isoniazid with riboflavin added in this proportion has established that riboflavin may be used as a means of detecting those patients who have ingested isoniazid less than twenty-four hours prior to the test. In the experiments described herein, the concentration of riboflavin in normal urine was equal to or less than 2·5 γ per ml. in essentially all instances. The concentration in patients receiving isoniazid in dosages equivalent to 5 to 10 mg. per kg. of body weight, with riboflavin added, *i.e.* in dosages equivalent to 0·8 to 1·6 mg. per kg., exceeded 2·5 γ per ml.

"The results of these studies indicate that riboflavin-tagged isoniazid is a practicable method for separating the patients who regularly follow self-medication programmes from those who do not."

EVANS, D. A. P., MANLEY, K. A. & MCKUSICK, V. A. **Genetic Control of Isoniazid Metabolism in Man.** *Brit. Med. J.* 1960, Aug. 13, 485–91, 2 figs. [28 refs.]

"Plasma isoniazid concentrations have been determined chemically six hours after drug ingestion in 484 subjects. The frequency distribution curve of these concentrations is bimodal. Individuals are divided by the antimode into rapid and slow inactivators of isoniazid. There is no heterogeneity for these characters due to sex or age, and on the numbers studied the distribution of phenotypes appears to be the same in American negroes as in whites. The numbers of subjects studied are too small to determine whether tuberculosis affects one phenotype more than another.

"267 of the subjects studied constitute 53 white families. The family data support the hypothesis that the slow-inactivator character is recessive. A 'dosage' effect of the allele controlling the dominant character is demonstrable in that there is a significant difference between the mean plasma isoniazid concentration of recognizable heterozygotes and the mean value of all other rapid inactivators.

"Possible reasons for the maintenance of the polymorphism are discussed, and so also are the therapeutic implications of this genetically determined isoniazid inactivator character."

PETERS, J. H., with the technical assistance of R. LARSEN & A. TABRI. **Studies on the Metabolism of Isoniazid. II. The Influence of Para-Aminosalicylic Acid on the Metabolism of Isoniazid by Man.** *Amer. Rev. Respiratory Dis.* 1960, Aug., v. 82, No. 2, 153–63, 5 figs. [22 refs.]

SBRAGIA, S. Osservazioni cliniche sulla possibilità de impiego nella terapia della tubercolosi polmonare di un nuovo derivato dell'isoniazide: il 2 carbossibenzal-isonicotinil-idrazone. [**Clinical Observations on a New Derivative of Isoniazid: 2 Carboxyl-Benzal-Isonicotinil-Hydrazone for Pulmonary Tuberculosis**] *Lotta c. la Tuberculosi.* 1960, Mar.–Apr., v. 30, Nos. 3/4, 255–69, 8 figs.

The new synthetic drug was combined with vitamin B6, to make up for increased elimination due to isoniazid, in a preparation called Euniazide and made by Eufarma of Florence. It was given to 10 patients for a period of 3–4 months and the author reports briefly on each case. The trial has confirmed that *in vivo*, as had already been demonstrated *in vitro*, this new drug has a useful action.

The sputum of 6 of the patients was bacteriologically positive before the trial; after taking the drug 3 turned negative, the bacilli in another became very scanty and were only to be found after enrichment techniques; 2 other patients remained positive. All patients produced less sputum after taking the drug. Pyrexia had been present in 6 patients and disappeared under treatment with the drug, which brought about a marked improvement in the general condition of all the patients. On the X-ray appearance, patients with recent disease are expected to derive most benefit from this new synthetic drug.

There were no signs of intolerance, and no evidence of any effect on hepatic function or other undesirable side effects; blood and urine were kept under observation by appropriate tests throughout the trial.

J. Cauchi

GRIFFITH, A. H. **Multiple Puncture BCG Vaccination using 35 Months Old Freeze-Dried Vaccine.** *Tubercle.* 1960, June, v. 41, No. 3, 178–80.

British freeze-dried BCG vaccine (Glaxo) prepared 35 months previously and stored for 33 months in a refrigerator but occasionally subjected to room temperatures was used for the vaccination by multiple puncture of 55 non-reactor schoolchildren aged 13–14 years. The strength of the vaccine was 50 mgm./ml. Vaccination was done with 18 needles set to penetrate the skin to 2 mm. through 2 separate drops of vaccine.

The vaccination lesions were inspected 95–100 days after vaccination and the children were tuberculin tested (Heaf's method). The lesions were classified as measuring under 1 mm., 1–1·5 mm. and 1·5–2 mm. in diameter. Neither confluence nor ulceration were seen. The results were:

BCG lesion	*No. of children showing various grades of Heaf reaction*				*Total No.*
Diameter	Negative	I	II	III	
1 mm.	0	4	6	2	12
1–1·5 mm.	0	6	23	3	32
1·5–2 mm.	0	1	8	2	11
Total	0	11	37	7	55

These results show that Glaxo freeze-dried vaccine retains its allergenic potency when stored for almost 3 years and that BCG vaccination by multiple puncture is followed by a satisfactory rate of tuberculin conversion. [See also this *Bulletin*, 1959, v. 34, 623, 879.]

H. G. Calwell

COMSTOCK, G. W. **BCG Vaccination.** [Correspondence.] *Tubercle.* 1960, June, v. 41, No. 3, 227–9.

As a result of BCG vaccination trials carried out by the United States Public Health Service in Puerto Rico, Georgia and Alabama it was concluded that tuberculosis in the vaccinated groups compared with the controls was reduced by only 30% [PALMER *et al.*, this *Bulletin*, 1959, v. 34, 879]. POLLOCK however [this *Bulletin*, 1960, v. 35, 565] suggested that complete follow-up of both groups could have led to an observed reduction of 80% in the incidence of tuberculosis in those vaccinated.

Comstock replies that there is no evidence of bias in the reporting of cases in the study population as implied by Pollock. He presents the figures again, showing that in Puerto Rico there was a reduction in tuberculosis among those vaccinated of 30·9% and in Georgia and Alabama of 35·9%

He argues that if there was a true reduction of 80% in tuberculosis among the vaccinated as was found in the Medical Research Council's Trial in England [this *Bulletin*, 1956, v. 31, 621; 1960, v. 35, 253] and an observed reduction of only 30% the difference cannot be due to incomplete notification for if it were many more cases must have been missed among the controls than among the vaccinated. If the notification system were perfect in identifying cases among the vaccinated it would have to fail to identify 70% of cases among the controls, and if it failed to identify half of the cases in the vaccinated groups it would have to fail for 85% of the cases in the controls.

Comstock gives details of the measures adopted to avoid bias. Both the vaccinated and control groups in Georgia and Alabama were similar with respect to the proportion followed up, and both groups in the whole study were similar with respect to age, sex, residence and initial tuberculin sensitivity. There was no evidence of over-diagnosis of tuberculosis. It is Comstock's conclusion that the different results obtained in the British and the American trials have not arisen from technical features in the experimental designs of the trials but from "biologic or epidemiologic" differences.

H. G. Calwell

SERGENT, Ed., CATANEI, A. & DUCROS-ROUGEBIEF, Henriette. Prémunition antituberculeuse par le BCG. Campagne contrôlée poursuivie à Alger depuis 1935. Troisième note. [**Anti-Tuberculosis Campaign with BCG in Algiers, Followed Up Since 1935. Third Note**] *Arch. Inst. Pasteur d'Algérie*. 1960, June, v. 38, No. 2, 131–7.

The main features of the trial of oral BCG vaccination in the newborn in Algiers [see this *Bulletin*, 1954, v. 29, 1147, and 1957, v. 32, 569] are (1) a concurrent control series of equal size, chosen completely at random from the same very poor environment; (2) the evaluation of the results in terms of the mortality from all causes; (3) observation of all subjects every 6 months for an indefinite period. Those vaccinated at birth were re-vaccinated orally in their first, third and seventh year of life. By the end of 1958 the subjects, who were all born during the years 1935 to 1947, had been followed up into their eleventh year of age, and a further year was allowed to elapse, to assist in the discovery of defaulters, before the results were compiled for the 11-year period.

The original series of 21,240 vaccinated and 20,062 controls have diminished, by deaths (about 6,000 in each group), losses from observation (of the same order) and incidental vaccinations under the International Tuberculosis Campaigns (843 in the originally vaccinated and 1,006 in the control group) to 7,930 vaccinated and 6,594 unvaccinated, all observed during their eleventh year.

The death rates from all causes year by year show the following percentages of excess mortality in the unvaccinated compared with the vaccinated group:

Year of age	*Percentage excess mortality from all causes in unvaccinated group over vaccinated group*
1st	3
2nd	18
3rd	45
4th	88
5th	91
6th	65
7th	115
8th	64
9th	48
10th	64
11th	36

The figures for the first 7 years differ slightly from those previously published owing to the rediscovery of children earlier thought to be lost. *Ian Sutherland*

VENEREAL DISEASES

BIRENBOIM, H. L. & GOBLE, M. L. **Venereal Diseases in the Far East. Evaluation of Therapy.** *U.S. Armed Forces Med. J.* 1960, June, v. 11, No. 6, 665–70.

These authors treated 65 cases of gonorrhoea, 40 of non-gonococcal urethritis and 24 of chancroid in a troop-ship travelling from Japan and Korea to Seattle, Washington, the voyage lasting 144 days; all patients therefore were under close observation until they disembarked.

The penicillin treatment of gonorrhoea varied from 600,000 units of procaine penicillin G once a day for 3 days to 1,200,000 units twice a day for 3 days [a somewhat excessive dosage]. Of 54 patients receiving the minimum dosage 47 were cured, 2 developed non-gonococcal urethritis and were cured with aureomycin and 5 required doses up to the maximum; of 11 patients with a history of penicillin sensitivity 10 were cured by aureomycin and 1 by oxytetracycline.

Of the 40 patients with non-gonococcal urethritis 3 were cured by erythromycin and of 37 treated with Gantrisin (sulfisoxazole), 3 gm. at once and 1 gm. 4 times a day for 5 days, 26 were cured and 11 failed; 6 of the 11 were cured by aureomycin and 5 by erythromycin. [This success rate is remarkably high and has not been equalled in Great Britain.]

24 patients with chancroid were all cured by Gantrisin, 3 gm. at once followed by 1 gm. 4 times a day for 5 days.

[It would be interesting to know what serum levels of penicillin were reached with the 3 different dosages of penicillin, particularly the largest.] *T. E. Osmond*

GUTHE, T. **The Treponematoses as a World Problem.** *Brit. J. Venereal Dis.* 1960, June, v. 36, No. 2, 67–77, 5 figs.

This is an article of absorbing interest telling as it does of the progress made in tackling the various treponematoses, yaws, syphilis (including the endemic form) and pinta. When one realizes that 15 years ago there were in the world 50 million cases of yaws, 20 million of venereal syphilis, 1 million of non-venereal endemic syphilis, and an unknown number of pinta, the size of the problem is apparent. Whether these are the same or different diseases is largely of academic interest since all react to penicillin and, where treatment is applied to all, the disease can be wiped out as it has been in Bosnia.

In various tables and figures are set out the common features of the diseases, the trends of gonorrhoea and syphilis in the various parts of the world over the last 15 years and the work done in yaws campaigns: in these 70 million people were examined in surveys, 90 million in re-surveys and 30 million treated; a map shows the geographical distribution of endemic syphilis, yaws and pinta.

Syphilis seems more difficult to control than yaws though there has been a fall to 15–20% of its peak of a few years ago; however it seems to be increasing in some civilized countries in spite of control measures; it will surprise many to read that in Ethiopia as many as 30–60% of those between 15 and 60 years gave positive serum reactions. It is intriguing to note that there has been no similar trend in gonorrhoea though it reacts to similar treatment. It should be possible to eradicate yaws given the necessary facilities which demand a co-ordinated overall plan to which all countries subscribe. One danger which must be remembered is the possibility of yaws being replaced by venereal syphilis as civilization advances in the more backward countries.

The role of WHO is to encourage and co-ordinate the efforts of the various voluntary organizations, health administrations and other societies and especially to stimulate research both nationally and internationally; we still cannot cultivate treponema pallidum and we still cannot distinguish this organism from *T. pertenue* and *T. carateum*; it is quite remarkable how little is known about pinta. *T. E. Osmond*

WILLCOX, R. R. **Evolutionary Cycle of the Treponematoses.** *Brit. J. Venereal Dis.* 1960, June, v. 36, No. 2, 78–91, 2 figs. [Numerous refs.]

This long article is of absorbing interest, more especially so as the author has studied these diseases in many parts of the world.

The diseases considered are syphilis, both venereal and non-venereal (endemic), yaws, and pinta; little is said about this last because very little is known [one wonders why]; endemic syphilis is known by a number of different names according to the locality in which it occurs. Whether all these forms are the same disease has not yet been decided; they have many points of similarity but also show numerous differences; the proponents of the unitarian theory hold that environmental conditions, climate, standards of living, etc. can explain them. Endemic syphilis is non-venereal and can be spread by direct contact *e.g.* kissing or by animate and inaminate objects; it is never or hardly ever congenital; the same applies to yaws. Children readily become infected particularly those between 6 and 12 years of age; genital chancres are very rarely seen. The conditions which favour the spread are primitive living conditions, social habits and customs, trauma, climatic conditions and malnutrition; those affected are usually, but not always, immune to venereal syphilis. The clinical picture may be modified by both environmental and host factors; negroes tend to develop annular eruptions, cardiovascular lesions and gummata, but neurological involvement particularly tabes and GPI are much rarer in endemic than in venereal syphilis.

As civilization advances endemic syphilis tends to revert to the venereal form partly at any rate as a result of treatment and improved social conditions; the opposite however may occur especially after a serious and widespread calamity. The history of syphilis is briefly considered; the author evidently inclines to the pre-Columbian theory but agrees that the matter is still undecided. The evolutionary cycle of treponematoses is well shown in a figure; primitive social conditions with all that goes with them favour persistence of endemic syphilis; improved ways of life together with penicillin treatment can almost completely eradicate the disease (as it did in Bosnia) but as long as transmission factors exist there is a danger of deterioration should the same or another treponematosis be introduced or re-introduced. There is a good deal of cross immunity between the various forms of the disease but it is by no means complete and superinfection is not so very rare. Until virulent spirochaetes can be cultivated and the unity or otherwise of the various forms decided the problem will remain; much research is needed before the conquest of syphilis is achieved. *T. E. Osmond*

RAM, L. M. **Treponematosis in Singapore.** *Brit. J. Venereal Dis.* 1960, June, v. 36, No. 2, 93–7, 1 fig.

Yaws has probably been endemic in Malaya from the early times of unrecorded history; in the period 1954–58, 511,603 people were examined and 63,209 cases (12%) were found: in Singapore in the 4 years up to 1958, 65, 53, 9 and 15 cases respectively were diagnosed.

In Singapore syphilis appears to have been entirely imported; in 1819 the entire population was 150 but this has risen to 1½ million (75·4% Chinese and 13·6% Malayasians), in 1957. Legislation has been much the same as in Great Britain; brothels were abolished in 1930. The number of cases of early syphilis fell from 5,166 in 1927 to 116 in 1955 but rose to 174 in 1958; the corresponding numbers of all cases of venereal disease were 14,106, 5,088 and 5,233; during the whole period the population increased from ½ million to 1½ million.

Known cases of marital syphilis were 3,337 in 1958, wives being more often infected than husbands in the proportion of 72 to 54; infantile syphilis fell from 140 in 1950 to 8 in 1958; ante-natal syphilis fell from 5·4% of those examined in 1951 to 0·7% in 1958.

In 1958, 132 cases of late symptomatic syphilis were

seen including 39 skin, bones and joints, 19 cardiovascular syphilis, 16 GPI, 3 tabes and 55 other neurosyphilis. From 1954 to 1958 the total number of syphilis patients attending clinics fell from 1,896 to 1,035; during this period neurosyphilis has increased from 35–56% while syphilis of skin, bones and joints decreased from 50 to 29%. Results of treatment with penicillin are much the same as elsewhere (90% cure in early and 40% in late latent cases); reactions were also similar—only 1 death being recorded in the last 5 years. In 1958, 594 prostitutes attended clinics comprising 39 early and 75 late syphilis, 169 mixed infections with syphilis, 170 gonorrhoea and 141 no disease.

T. E. Osmond

HAMELIN, A. & VAISMAN, A. Étude comparative des réactions avec antigènes tréponémiques et lipidiques dans le liquide céphalo-rachidien. [**Comparative Studies on Reactions to Treponemal and Lipid Antigens in Cerebrospinal Fluid**] *Ann. Inst. Pasteur.* 1960, June, v. 98, No. 6, 924–7.

A comparative study was made of reactions with treponemal and lipoid antigens on the cerebrospinal fluid.

These authors tested 345 cerebrospinal fluids (CSF) by means of 4 tests (1) TPI (2) Wassermann with cardiolipin (B–W cardiolipin) (3) Wassermann with Reiter antigen (RPCF) and (4) Wassermann with virulent treponemal antigen (TPCF).

In 273 cases all 4 reactions were negative and in 60 all were positive; in 12 RPCF and TPCF were both positive, TPI was positive in 4 and weakly positive in 2 and BW cardiolipin was positive in 2 and doubtful in 1.

It was established that in active neuro-syphilis all reactions are positive but in patients treated, stabilized or cured the RPCF and TPCF often remain positive when the others have reverted to negative; the B–W cardiolipin is less sensitive than the other tests but is highly specific.

Results of the 4 tests on the 12 discordant cerebrospinal fluids are set out in a table. [No information is given as to the sources of the cerebrospinal fluids; the status of patients whose fluids were negative with TPI and positive with RPCF and TPCF would be interesting.] *T. E. Osmond*

SCIPLE, G. W., MONTGOMERY, C. H. & KNOX, J. M. **Diagnostic Problem related to a "Biologic False-Positive" Serologic Test for Syphilis.** *New England J. of Med.* 1960, July 14, v. 263, No. 2, 84–5.

The problem was that of a 14-year-old boy who gave a routine positive serum test for syphilis; the father, mother and 10 siblings were all sero-negative. Further investigations showed that the mother had received intravenous injections for a rash on the face and palms 3 months before the birth of the child and the father 6 similar injections for a penile ulcer several months before his wife's illness. Further investigations revealed the following results of tests:—the patient VDRL weakly reactive, Kolmer WR ("serum Kolmer test") reactive, Kahn negative, Reiter protein complement-fixation test (RPCF) reactive, TPI reactive and Kolmer complement-fixation test negative; the mother showed reactive Kolmer WR, RPCF and TPI tests but the other tests negative; the father showed a weakly reactive TPI but other tests negative; 10 siblings all gave negative VDRL tests. On the strength of these results the boy was diagnosed as a case of congenital syphilis. [It is not clear what is the difference between "serum Kolmer test" and "Kolmer complement-fixation test".]

T. E. Osmond

BERLIN, C., TAGAR, A., EYLAN, E. & LINDENBAUM, I. [**Clinical and Serological Findings in Syphilis in relation to the Nelson Test**] *Harefuah.* Jerusalem. 1960, Aug. 15, v. 59, No. 4, [in Hebrew 107–8. English summary 108].

The English summary appended to the paper is as follows:—

"A survey is given of 250 cases examined for syphilis during the 2½ years, 1957–1960. The patients were examined clinically and serologically with the standard serological and Nelson tests.

"None of the 250 cases examined showed fresh symptomatic or latent syphilis. 118 cases were in the late and latent period, 7 had visceral syphilis, 25 showed affection of the nervous system and 14 had late hereditary syphilis. The disease was questionable in 23 cases. It was shown that 63 cases (25%) had no syphilis in spite of the positive serology. The importance of the treponema immobilization test for the specific diagnosis of serologically positive cases was stressed."

PORTELLA, O. B. & THOMPSON, W. R. **Quantitative Studies of the *Treponema* Immobilization Reaction. II. Determination of Potency of Strongly Reactive Sera, Comparison of Reference Standards, and Preparation of a Replicate Standard.** *Immunology.* Oxford. 1959, Oct., v. 2, No. 4, 295–308, 3 figs. [13 refs.]

At first sight this article looks like a study in higher mathematics; moreover it is both complicated and technical. No adequate abstract therefore is possible in a few words and the article should be studied in the original by those few who are interested.

Briefly, the authors discuss and estimate the various WHO reference sera for use in the TPI test and show that a pool of reactive rabbit sera or of human sera answers the purpose equally well.

[For an earlier study by the authors, see this *Bulletin*, 1958, v. 33, 120.] *T. E. Osmond*

MONTGOMERY, C. H., SUHRLAND, Sylvia & KNOX, J. M. **Behavior of the Fluorescent Treponemal Antibody Test in Early Syphilis.** *Pub. Health Lab.* 1960, May, v. 18, No. 3, 44–8.

The fluorescent treponemal antibody test (FTA) was run in parallel with the Reiter protein complement fixation test (RPCF) and the VDRL test on sera from

patients with primary, secondary and latent syphilis, treated and untreated.

In primary syphilis (58 cases) all tests were positive in 22 and all negative in 4; in 19% FTA alone was positive; in 27·6% RPCF was the only negative one.

In 34 secondary cases FTA and VDRL were positive in all, but RPCF was negative in 23·5%.

In 35 cases of latent syphilis, in 82·9% all tests were positive, 2 were negative with FTA and 4 negative with RPCF.

As regards relative sensitivity FTA was positive in 91·4% of primary, 100% of secondary and 94·3% of latent cases: the corresponding figures for VDRL were 65·5, 100 and 100, and for RPCF 46·6, 76·5, and 88·6. These qualitative results were highly reproducible but when quantitative tests were carried out results fluctuated considerably [the authors attribute this to poor technique].

After treatment FTA titres fell but not as rapidly as with VDRL; in some cases of early syphilis FTA titres rose and this was most common in latent cases; in primary cases after 6 months only 12·8% of FTA tests became negative compared with 80·6% for VDRL and 74·2 with RPCF; in secondary cases FTA gave 0 compared with 20 for VDRL and 60 for RPCF; in latent cases the respective figures were 0, 21·4 and 39·2. Thus the FTA test appears valuable in early syphilis but less valuable in treated cases [it would be interesting to compare it with TPI in these latter]. *T. E. Osmond*

GENERAL INFECTIVE DISEASES

The order in this section is:—**General; Hospital and Other Cross Infections; Coccal Infections; Bacterial Infections; Virus Infections.**

GENERAL

MORAES, N. L. de A. Importância sanitária das diarréias infantis no Brasil. [**Hygienic Importance of Infant Diarrhoea in Brazil**] *Rev. Serviço Especial de Saúde Pública.* Rio de Janeiro. 1959, Dec., v. 10, No. 2, 707–14. [10 refs.]

The English summary appended to the paper is as follows:—

"Basing his study on available data, the author estimated that Brazil had 1,100,000 to 1,400,000 infant deaths from 1950 to 1959 resulting from infectious diarrheas, concluding that this group of diseases constitutes the main cause of morbidity and mortality among Brazilian children."

MAROJA, R. de C. & SANCHES DE ALMEIDA, A. Diarréias infectuosas e desnutrição. [**Infectious Diarrhoea and Malnutrition**] *Rev. Serviço Especial de Saúde Pública.* Rio de Janeiro. 1959, Dec., v. 10, No. 2, 715–32, 4 graphs. [32 refs.]

The English summary appended to the paper is as follows:—

"The authors analyze up-to-date knowledge about diarrheal diseases in infancy and discuss, besides other points, the possible association between this group of diseases and the social economic level of the population, including malnutrition. They also comment on the lack of conclusive data and the complexity of the above subject.

"They show that infant mortality in the north-east of Brazil is caused chiefly by infectious diarrheas. They indicate that such mortality is responsible for low expectancy of life at birth. However, once children reach their first anniversary, longevity is similar to that occurring in the south of the country.

"The authors add that the Serviço Especial de Saúde Pública (SESP), considering the importance of the problem, is promoting surveys trying to discover if there is some correlation between diarrhea and water used in homes, intermediate and final disposal of human excreta, and the role of flies in the spread of these diseases.

"Cases found are under clinical and therapy control, and the social-cultural conditions of the families included in the survey are noted.

"Finally, the authors inform that infant mortality has decreased, some Northeastern areas having better medical-sanitary services without parallel economic improvement."

PETERSEN, N. J. & HINES, Virginia D. **The Relation of Summertime Gastrointestinal Illness to the Sanitary Quality of the Water Supplies in Six Rocky Mountain Communities.** *Amer. J. Hyg.* 1960, May, v. 71, No. 3, 314–20.

Gastro-intestinal illness in those who visit countries foreign to their own is well recognized [this *Bulletin*, 1960, v. 35, 264]. No definite aetiological agents have as yet been discovered. There are many instances in the literature in which reported outbreaks of enteric disease have been attributed to contaminated water supplies. In the present paper there is an account of a morbidity survey made in 1957 of 6 Rocky Mountain communities "to determine whether a correlation existed between the sanitary quality of the water supplies and the incidence of unreported summertime gastrointestinal illness in the populations using these supplies".

3 of these communities consumed untreated surface water and the other 3 had adequately treated water supplies. Records of the water analyses of these 6 communities were available in the State Health Department and the quality of the waters was evaluated by bacteriological criteria which are stated. House-to-house

visits were paid to about 100 families in each community to obtain retrospective information on the incidence in the summer months of gastro-intestinal illness which was defined as a sudden onset of watery diarrhoea with or without nausea and vomiting with symptoms persisting for at least 1 day.

The results are fully described with numerical tables on water quality during 3 years; the diarrhoea attack rate by age, month and family; attack rate by length of residence in each area and clinical particulars.

It was found that (1) populations served by consistently contaminated water suffered an attack rate of 14% during the 3 summer months as compared with 9% in the other communities with satisfactory water supplies; the diarrhoea in the former communities was more severe than the illness in the good water areas; and (2) the attack rate among people who had been exposed less than 2 years to contaminated water was twice that of people so exposed for a longer period.

M. E. Delafield

BUTLER, N. R. & BARR, Mollie. **Combined Immunization against Diphtheria and Tetanus with Three Types of Prophylactic.** *Med. Officer.* 1960, Jan. 22, v. 103, No. 4, 41–2.

This paper records the results of trials of two diphtheria-tetanus prophylactics, one a mixed preparation of purified toxoids adsorbed on aluminium hydroxide and the other without any mineral carrier. Both contained diphtheria toxoid 60 Lf/ml. and tetanus toxoid 10 Lf/ml. plus the usual suitable excess. Results are also given of a follow-up study of children immunized in infancy with diphtheria-tetanus-pertussis prophylactic as a plain unadsorbed preparation [this *Bulletin*, 1956, v. 31, 363].

The results obtained, with the inoculation programme followed, showed that the triple prophylactic given at 12, 16, 20 and 52 weeks is an efficient preparation, adsorbed diphtheria-tetanus toxoid given at 12 and 20 weeks of age also gave promising antibody levels, but diphtheria-tetanus without a mineral carrier or the admixture of pertussis vaccine is a weak prophylactic for primary immunization but is suitable for reinforcing immunity.

H. J. Bensted

PAVLOV, P. V., AKIMOVA, V. V., ANANASHCHENKO, N. I. & ATSEROVA, I. S. **Experimental Studies of the Antigenic and Immunogenic Properties of Combined Vaccine against Scarlet Fever, Diphtheria and Pertussis.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 5, 51–8. [Translated from Russian.]

Triple scarlet fever-diphtheria-pertussis, both adsorbed and unabsorbed, prophylactics were prepared and tested for immunogenicity, and suitability for subsequent use in children, in experimental animals by antibody response in guineapigs and rabbits and protection tests in mice. The triple antigen was prepared as for use in children and most of the preparations tested contained 15,000 skin test doses of scarlet fever toxin, 30 Lf diphtheria toxoid and 20,000 × 10^6 whooping cough bacilli in 0·5 ml. It is reported that the immune responses in the experimental animals were good and that there was no evidence of interference between the components.

Although the diphtheria antitoxin levels were higher after the first dose of the adsorbed preparation than with the unadsorbed this difference was ironed out subsequently. In view of the possible untoward effects of immunizing children with the triple antigen containing a mineral carrier it was considered, since there was no essential difference in the immunizing properties of the two vaccines at the end of the course of injections, that the unadsorbed preparation would be more suitable.

The authors give no information about the incidence of scarlet fever in the U.S.S.R. to explain the inclusion of scarlet fever toxin in the combined prophylactic but they indicate that groups of children in Leningrad and Vologda have been immunized with an adsorbed purified scarlet fever toxin with satisfactory immunological and epidemiological results.

H. J. Bensted

UNITED STATES DEPT. HEALTH, EDUCATION & WELFARE. **Immunization Information for International Travel. Prepared by Epidemiology and Domestic Operations Branch, Division of Foreign Quarantine of the Bureau of Medical Services.** *Pub. Health Service Publication No. 384.* Revised May 1960. 83 pp., 3 maps. Wash. 25: U.S. Govt. Printing Office, D.C., U.S.A. [$0.25.]

[See this *Bulletin*, 1959, v. 34, 105, 1960, v. 35, 259.]

HOSPITAL AND OTHER CROSS INFECTIONS

HOFSTAD, T. & VOGELSANG, T. M. **Pathogenic Staphylococci in the Upper Respiratory Tract. Their Occurrence in Patients in a Medical Department.** *Acta Med. Scandinavica.* 1960, July 15, v. 167, No. 4, 279–85, 1 fig. [25 refs.]

During a 4-month period 164 female and 133 male patients in medical wards in a Bergen hospital had nose and throat swabs examined on admission and twice weekly thereafter. The total carrier rate for *Staph. aureus* rose from about 50% on admission to about 80% by the 6th week; the carrier rate for resistant staphylococci rose from about 10% to over 30%. Patients who were initially non-carriers acquired resistant strains more often than those originally carrying penicillin-sensitive staphylococci. 33% of the penicillin-resistant staphylococci were phage-group I (either 80 or 52/52A/80) and 57% were group III. 19 of the 297 patients had staphylococcal disease; in 6 it was acquired in the ward, in 7 in other departments of the hospital, and in 6 outside the hospital.

R. E. O. Williams

FORTUNATO, A. & SEPE, E. Ricerca dei portatori di stafilococchi, tra il personale dell'Ospedale Ascalesi di Napoli. [**A Search for Staphylococcal Carriers amongst the Staff of the Ascalesi Hospital in Naples**] *Ann. Sclavo.* Siena. 1960, May–June, v. 2, No. 3, 201–12. [26 refs.] English summary (9 lines).

Nasal swabs were taken from the 91 members of the nursing staff and seeded on to Chapman Stone medium "Difco", which brings out well pigment characteristics and gelatinase activity. Coagulase tests, haemolytic action, mannite fermentation and sensitivity to 7 antibiotics were studied.

All the staff were found to be harbouring staphylococci, 61 carrying coagulase positive strains and 58 carrying *Staph. aureus.* 86·8% of the coagulase-positive strains were resistant to penicillin and 40·9% to streptomycin, while only 1 strain resisted chloramphenicol, which appears to be the most active of available drugs, possibly because it is used most sparingly. Resistance to more than 3 antibiotics seemed to be more widespread among coagulase-negative strains. The authors gathered there was no increased incidence of staphylococcal infections in the hospital at the time of their investigation.

E. Agius

HARVEY, H. S. & DUNLAP, Marjorie B. **Upper Respiratory Flora of Husbands and Wives. A Comparison.** *New England J. of Med.* 1960, May 12, v. 262, No. 19, 976–7.

Nose and throat cultures were taken from 75 married couples and examined for various bacterial species. The percentage of couples, respectively, with 1 or other member positive and with both positive were: haemolytic streptococcus 36 and 12, pneumococcus 34 and 11, staphylococcus in throat 37 and 12, coliform organisms 30 and 4, yeasts 13 and 3; *Haemophilus influenzae* 67 and 51, and *H. haemolyticus* 67 and 48. There does not, therefore, seem to be any great tendency for husbands to carry these organisms at the same time as their wives, or *vice versa.*

R. E. O. Williams

MACHADO, E. M., SOLÉ-VERNIN, C., ULSON, Cecilia M., GOUVEIA, F. P., CONCEIÇÃO, J. A. N., COELHO, Hebe da S., NEVES, F. de P., Jr. & DA SILVA, J. A. Estudos sôbre as estafilococcias. II. Incidência de portadores entre crianças hospitalizadas; antibiograma e fagocitagem das amostras obtidas de colheitas semanais. [**Studies on Staphylococcal Infections. II. Carrier Incidence among Hospitalized Children; Antibiogram and Phage Type of the Strains isolated from Weekly Specimens**] *Rev. Inst. Med. Trop. São Paulo.* 1960, May–June, v. 2, No. 3, 131–9, 1 fig. [21 refs.]

The English summary appended to the paper is as follows:—

"The authors observed the carrier state of 12 children who were admitted for the first time to the Paediatric Ward of a General Hospital taking nose and throat exudate for the isolation of coagulase-positive staphylococcus, at weekly intervals during 9 weeks. The isolates were phagetyped (courtesy of Dr. R. E. O. Williams) and their sensitivity to 11 antibiotics was estimated. Only one of the children was consistently negative during the whole period of observation. Four of them were already carriers at the moment of admission, and, curiously enough, their phagetypes were 80 and 81. With regard to constancy of phagetype colonization, only four of the children could so be considered, although this did not occur from the first exudates. Twelve phagetype patterns were present with greater frequency of 75 (44·6%), 80 (16·1%) and 52/80 (16·1%). The mean antibiograms for these three phagetypes showed greater sensitivity to the antibiotics før phagetypes 80 and 52/80, than for phagetype 75; this later one is characterized by great resistance to penicillin, streptomycin, chloramphenicol and tetracycline."

BARALT-PEREZ, Josefina, HADDOCK-SUAREZ, J., AXTMAYER, A. L. & RODRIGUEZ-MOLINA, R. **Phage Typing and Antibiotic Sensitivity of Staphylococcci from Hospital Patients and Personnel.** *Bol. Asoc. Med. de Puerto Rico.* 1960, July, v. 52, No. 7, 215–21.

"1. One hundred and forty-eight (45.8%) individuals among 323 members of the personnel of the VA Hospital in San Juan, Puerto Rico, gave positive cultures of coagulase producing staphylococci. Seventy-three per cent (73%) of the strains isolated were phage typable. Of these, 48.7% belonged to Group III and 18.8% to type 80/81.

"2. Seventy-nine per cent (79%) of 100 coagulase positive cultures from different sites of infection in patients were typable. Among these, type 80/81 (41.8%) and Group III (39.2%) predominated.

"3. Antibiotic resistance was significantly higher among 80/81 strains isolated from patients; a high degree of resistance to penicillin as well as to the tetracyclines and dihydrostreptomycin was observed.

"4. Results obtained confirm observations made by investigators elsewhere."

WALDTON, S. Luftbakteriehalten på ett centrallasaretts operationsavdelning, speciellt under pågående operation. [**Airborne Bacteria in an Operation Department of a Central Hospital, particularly during Operations**] *Nordisk Med.* 1960, Sept. 1, v. 64, No. 35, 1089–91, 2 figs. [17 refs.]

The English summary appended to the paper is as follows:—

"The amount of airborne bacteria in the operation department of the Hospital of Falun, Sweden, has been studied with BOURDILLON'S slit sampler. A report is given of the results from 81 air samples taken in the morning in undisturbed operating theatres and from 27 operations, of which 10 were performed with open windows. The results show little effect of sterilamps, partly depending

on the fact that the method of sampling mainly collects dust particles in undisturbed rooms (in comparison with droplets). Ventilation through open windows (in summer) during an operation could be allowed, since it was as good as or better than the local ventilation system. Theatres with so-called 'unclean' operations did not show a higher content of airborne bacteria than did other theatres. Cleaning of the operating theatres in the morning had no demonstrably favourable effect on the amount of airborne bacteria. Air-suction pumps equipped with double water-traps and filters did not produce any decisive increase of airborne bacteria."

MARTENSSON, E. H. Luftbakteriehalten på en operationsavdelning undersökt med sedimenteringsplattor. **[Investigation of Airborne Bacteria by Sedimentation Plates]** *Nordisk Med.* 1960, Sept. 1, v. 64, No. 35, 1092–5, 1 fig. [11 refs.]

The English summary appended to the paper is as follows:—

"Some main factors influencing the amount of airborne bacteria are briefly mentioned.

"Open Petri dishes with blood agar were repeatedly exposed for six hours to airborne bacteria in different rooms of the Surgical Operation Department in order to check the bacteriological conditions and to compare different localities with each other. Even with such a long time of sampling there are great variations in the number of colonies grown on the plates from one and the same room on various days. Yet, the mean values were considered to offer some evidence. Special interest was devoted to comparing two nearly equivalent rooms, one of which was equipped with sterilamps but not the other one. The first room showed a lower mean value of airborne bacteria which suggested a possible effect of the ultra-violet radiation, but the difference was not statistically significant. The limitations of the effectivity of such radiation in workrooms are stressed. A coarse reversed relationship between the means of the bacterial contents and the volumes of the rooms was found.

"Airborne bacteria were also examined with respect to their species, in most cases from the characters of the colonies. The results from several plates have been summarized, and the average values are given in table 1. The dominating group, 80–90%, consists of Staphylococcus albus, which mainly may be regarded as non-pathogenic. Most pathogenic organisms are to be found in the group containing Staphylococcus aureus (only a minor part) and haemolytic staphylococci. For practical reasons coagulase tests could not be performed, and in the author's opinion all of these strains are not true pathogens, although they may be biologically more active. In the material from 1958 the last-named group is reduced (5.6% as against 14.2% in 1956), which seems to indicate an improvement of the general conditions, though other factors may have contributed. The rest of the bacterial species were of minor interest as possible pathogens."

KNIGHTS, H. T. **Ward Cleaning Equipment and Aerial Contamination. Tests conducted upon the Electric Vacuum Polisher.** *New Zealand Med. J.* 1960, June, v. 59, No. 334, 291–3, 1 fig.

"An electric vacuum polisher has been tested by examining the air contamination during its use compared with that during the employment of the ordinary electric polisher. The results are given and the conditions of its employment suggested.

"Whereas there does not appear to be a great difference between the two plates, the counts in A employing the ordinary polisher are in actual fact more than double those of B where the vacuum polisher was used."

ROUNTREE, Phyllis M., HARRINGTON, Maureen, LOEWENTHAL, J. & GYE, R. **Staphylococcal Wound Infection in a Surgical Unit.** *Lancet.* 1960, July 2, 1–6, 1 chart. [13 refs.]

During a 6-month period in 1959, 217 surgical wounds in patients in a surgical unit in a Sydney hospital were studied to determine the incidence of clinical infection. Altogether 40 wounds became infected; the incidence of infection was 7% on 171 clean wounds covered with a plastic seal, 56% on 27 clean wounds covered with gauze and 68% on 19 initially "dirty" wounds covered with gauze. ["Infection" is apparently used to denote clinically manifest disease in initially clean wounds and bacteriological cross-infection in initially dirty wounds.] No very great difference in the incidence of infection could be related to the site of the operation or the operator.

6 of the 40 infected patients died; in one case death was apparently in part due to the infection. 2 patients suffered complete wound dehiscence and in 20 others stay in hospital was prolonged by an average of about 15 days. *Staphylococcus aureus* was isolated from 35 of the infected wounds; strains lysed only by phage 47 used at 1,000 times RTD were predominant.

Air samples taken in the operating theatre during use revealed an average of 10 colonies of bacteria per cu.ft., with only 0·013 colonies of *Staph. aureus*, many of which proved to be of the same type as those carried by the person operating the sampler. No evidence could be found that the wound infections were due to staphylococci carried by the surgical team in the theatre.

Patients and staff in the wards were commonly carriers of the dominant type 47 staphylococcus. There was some evidence that carriers of *Staph. aureus*, and particularly of the type-47 strains, developed wound infection with the same type as they had in their nose, though whether the wound was infected from the nose or elsewhere could not be determined. It was thought that 7 of the 35 patients with staphylococcal infection suffered autogenous infection with a strain present in their nose on admission to the ward; 12 had either autogenous or ward infection, the nose and wound staphylococci belonging to the same type but the type being common in the ward; 14 were presumed to be ward infections with no prior nasal colonization, and 2 were possibly theatre infections.

R. E. O. Williams

POOLE, Pauline M. **The Reinvasion of a Maternity Unit by** *Staphylococcus aureus*. *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1960, July, v. 19, 113–23, 1 fig. [16 refs.]

Studies were made of the introduction and spread of strains of *Staphylococcus aureus* in a maternity unit in the 6-month period following its reopening after closing and cleaning. The babies' umbilical stumps were painted with triple dye daily but no other chemoprophylaxis was used. Nasal and umbilical swabs were taken from 437 babies at about the 8th day of life; about 80% were then found to be nasal carriers and 20% umbilical carriers of *Staph. aureus*. 88% of the staphylococci were resistant to penicillin and 36% were resistant to oxytetracycline. 105 mothers had nasal swabs taken on admission to hospital and 32 were found to be carriers; in only 4 instances did their babies acquire strains of the mother's nasal type. Breast swabs were taken from 136 mothers on the 8th day after delivery; 24% yielded staphylococci of the type carried by the mother's infant.

726 strains of staphylococcus were tested for phage type; 92 were untypable and the remainder were distributed over 105 different types, 371 falling into one or other of 3 dominant types—52A/80, 52A/77 and 83A (all typable only at RTD × 1,000). These types were all introduced into the nursery, at the time it was reopened, by nurses who were nasal carriers. The first was constantly carried by nurses and colonized many babies; the third clearly spread among the babies in the absence of carriers among nurses. Another type, 6/7/47/54/75+, was also introduced by a nurse, but appeared unable to spread, and disappeared when she no longer carried it.

Follow-up swabbing of the babies after 3 and 6 months showed 43% and 37% to be nasal carriers; 32% and 15% respectively were apparently still carrying the hospital strain. *R. E. O. Williams*

ANDERSON, K., COULTER, J. & LOOKE, E. **Transfer of** *Staphylococcus pyogenes* **from Infected to Non-Infected Hospital Beds.** *Brit. Med. J.* 1960, June 25, 1925–7, 2 figs. [10 refs.]

In an 8-bed ward, all the beds were made up freshly with clean bedclothes and wool blankets; in one bed no sheets or pillowcases were used. This bed, and one of the conventionally equipped beds, was contaminated with broth cultures of *Staph. aureus*. The beds were remade twice daily and bacteriological samples were taken from each bed by a percussion technique daily but otherwise no one entered the ward. There was spread of staphylococci from the infected beds to the controls within the first few days, and spread seemed to occur equally readily from the contaminated woollen blankets and from contaminated cotton sheets.

[See also this *Bulletin*, 1960, v. 35, 996.]

R. E. O. Williams

CORNER, Beryl D., CROWTHER, S. T. & EADES, Sheila M. **Control of Staphylococcal Infection in a Maternity Hospital. Clinical Survey of the Prophylactic Use of Hexachlorophane.** *Brit. Med. J.* 1960, June 25, 1927–9, 1 fig. [18 refs.]

In a large maternity hospital in Bristol there were 3,721 live births in the year 1957–58 and 247 (7·4%) cases of pustular dermatitis; in the same period 50 (14·5%) of 344 premature infants developed skin sepsis. A new regimen was then introduced under which the babies had their cord-stump sprayed with "Octaflex" and their skin was dusted with a hexachlorophane powder each time the napkin was changed. In the subsequent year only 50 (1·5%) of 3,650 full-term infants and 9 (2·6%) of 352 premature infants developed pustular dermatitis. Inquiry of the general hospitals in Bristol indicated that the incidence of breast abscesses in the mothers might have fallen from about 2·4% to about 0·6%.

R. E. O. Williams

GREEN, R. T. B. **Notes on some Improved Measures in the Prevention of Staphylococcal Cross Infection.** Reprinted from *Roy. Perth Hosp. J.* 1960, June, Suppl., 3–12, 13 figs.

This is a general review article describing the problem of staphylococcal hospital infection and the routine adopted in the Royal Perth Hospital for its control. There is an interesting description of a wet "mat barrier" for use at the entry to sterile areas; the usefulness of this has not, however, been fully established.

R. E. O. Williams

COCCAL INFECTIONS

The order in this section is:—*Staphylococcus, Streptococcus, Neisseria, Others.*

MILLIAN, S. J., BALDWIN, J. N., RHEINS, M. S. & WEISER, H. H. **Studies on the Incidence of Coagulase-Positive Staphylococci in a Normal Unconfined Population.** *Amer. J. Pub. Health.* 1960, June, v. 50, No. 6, Pt. 1, 791–8. [26 refs.]

Nasal carrier rates were determined for *Staphylococcus aureus* in a random sample of 577 men and women selected from applicants for food-handling positions. They were 37% for 147 white females, 38% for 271 white males, 20% for 87 Negro females, and 10% for 72 Negro males. The difference between the white and Negro subjects is statistically significant. Sheep blood agar was found to be useful isolation medium; there was a high correlation between haemolysis on this medium and coagulase production. [The haemolysis is, however, unlikely to be due to the alpha-haemolysin as this is only produced when the cultures are incubated in an atmosphere of carbon dioxide.] *R. E. O. Williams*

SMITH, I. M. & VICKERS, A. Barbara. **Natural History of 338 Treated and Untreated Patients with Staphylococcal septicaemia (1936–1955).** *Lancet.* 1960, June 18, 1318–22, 4 figs. [29 refs.]

This is a review of the clinical and necropsy records of patients with staphylococcal septicaemia treated in the University Hospitals, Iowa, during the 20-year period 1936–55. The 338 cases include 69 of "secondary septicaemia" developing during another fatal disease. Apart from the "golden age" 1946–50 (presumably when penicillin was most active against prevailing strains of staphylococci) the incidence was more or less constant throughout the period. The ratio of male to female patients was 2 : 1, and the disease occurred in all age-groups but was commonest at the extremes of life. A distressing number of the infections were acquired in hospital. Among the 87 patients not treated with antibiotics the fatality rate was 90%. After 1950 the incidence rose but the fatality rate in treated patients fell, especially in those treated with penicillin plus sulphonamides.

Although the first blood culture was positive in the vast majority, a series of 3 blood cultures is recommended, where necessary, for diagnosis. The most frequent manifestation found at necropsy was haemorrhagic necrotizing pneumonia (107 cases); multiple kidney abscesses were the commonest lesions in the genito-urinary tract (39 cases); there were 26 cases of endocarditis, 18 of myocardial abscesses, and 14 of pericarditis; and in 16 necropsies meningo-encephalitis was the main lesion found.

Many of the patients succumbed to staphylococcal infection when they were debilitated by other conditions such as surgery, in the elderly, or when they were on a course of adrenal steroids. *H. Stanley Banks*

JAMES, W. E. S., BADGER, G. F. & DINGLE, J. H. **A Study of Illness in a Group of Cleveland Families. XIX. The Epidemiology of the Acquisition of Group A Streptococci and of Associated Illnesses.** *New England J. of Med.* 1960, Apr. 7, v. 262, No. 14, 687–94, 1 fig. [25 refs.]

During the study of minor illnesses among a group of families in Cleveland, Ohio, which has been the subject of several previous reports [this *Bulletin*, 1953, v. 28, 891; 1954, v. 29, 12], there were 490 occasions when an individual was found to have acquired a new group A streptococcus. 189 of the streptococci could not be typed; non-typable strains were acquired slightly more often by the adults than by the children. The total acquisition rate was 2·1–3·0 per 1,000 person days for schoolchildren; 1·6 for pre-school children from households with schoolchildren, and 0·4–0·6 for pre-school children and for adults. 43% of the streptococcal acquisitions were associated with illness typical of streptococcal infection compared with only 6% of a random sample of the individuals who acquired no streptococci. In the children, the proportion associated with illness was 58–66% for types 4 and 12 streptococci, compared with 35% for other types and 36% for untypable strains. The schoolchildren were responsible for 5 to 6 times as many introductions of new types into their families as the adults. Overall, there was a 25% secondary acquisition rate within the families after an introduction, but for the younger children the rate was as high as 50%. In some families the streptococci persisted for many weeks. *R. E. O. Williams*

SASLAW, M. S. & JABLON, J. M., with the technical assistance of Madelyn SAUL & Sallie A. JENKS. **Epidemiology of Group-A β-Hemolytic Streptococci as related to Acute Rheumatic Fever in Miami, Florida. A Six-Year Study.** *Circulation.* New York. 1960, May, v. 21, No. 5, Pt. 1, 679–83. [14 refs.]

This paper is largely a summing up of the several papers published by Saslaw and his colleagues over the past few years [see this *Bulletin*, 1957, v. 32, 88, 498; 1958, v. 33, 663; 1959, v. 34, 941, 1074].

In an extensive survey in Florida, group A streptococci were isolated from 11·1% of children aged 6–9 but from only 0·2% of their mothers and 2·2% of adults generally. On the other hand, the rheumatic fever register only recorded the occurrence of 83 active episodes of rheumatic fever in 3 years in a population of about 800,000. About half the children from whom group A streptococci were found in some small-scale studies developed a rise of antistreptolysin, but the association of clinical illness with streptococcal infection was not at all clear. *R. E. O. Williams*

HARKNESS, J. **"Epidemic" Nephritis in North Essex.** *Lancet.* 1960, July 16, 146–7.

In an investigation of a small outbreak of acute nephritis (4 cases) in a village school in Essex and in a boys' boarding school (2 cases) 28 of 277 people investigated proved to be carriers of *Streptococcus pyogenes* type 12 and 20 children were found to have symptomless urinary abnormalities. Oral penicillin given to carriers controlled the outbreak in the village school (these carriers were also excluded from school) but not in the boarding school where closer contact and possibly less thorough investigation may have been responsible for relative failure. *A. B. Christie*

BACTERIAL INFECTIONS

The order in this section is:—*General, Corynebacterium, Haemophilus, Enteric bacteria, Brucella, Pasteurella, Anaerobes, Spirochaetes, Others.*

TER-KARAPETIAN, A. Z. **Efficacy of Prophylactic Immunization with IEM Gamaleya Polyvalent Vaccine, Tetravalent Vaccine and NIISI Polyvalent Vaccine.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 7, 16–22. [Translated from Russian.]

The author does not indicate the composition of the vaccines given in the title of this paper, but presumably

they are well recognized in the U.S.S.R. and appear to be mixed vaccines for immunization against typhoid, paratyphoid and bacillary dysentery. The comparison of the 3 vaccines appears to have been based on the incidence of enteric and dysenteric infections in the 3 groups of inoculated subjects and the uninoculated group. A fourth vaccine—dysentery tablets—was also used for some part of the trials which extended over some 8 months. It is reported that the IEM Gamaleya Polyvalent and the NIISI polyvalent vaccines had about the same potency against typhoid with the Tetravalent vaccine somewhat less. The maximum efficiency began to wane about 4 months after inoculation. None of the vaccines had any protective effect against dysentery. *H. J. Bensted*

ANDRÉ, J., AUDEBAUD, G. & CHAMBON, L. Diagnostic de la diphtérie sur culture de tissu. [**The Tissue Culture Diagnosis of Diphtheria**] *Ann. Inst. Pasteur.* 1960, Aug., v. 99, No. 2, 179–87. [15 refs.]

Using the method of inoculation of cultures of monkey kidney cells for the detection of cytopathogenic viruses located in the throat the authors fortuitously observed that diphtheria toxin might be detected in this way. They got a marked destruction of the culture in one instance and being unable to propagate any virus in further subculture they traced the cause to the presence of *C. diphtheriae* in the throat of the patient who was a carrier of that micro-organism. The throat swab was allowed to soak in Hanks solution containing suitable amounts of penicillin, streptomycin, tetracycline and mycostatin and then 3 and 6 drops of this inoculum was transferred to the monkey kidney culture and 1 ml. of the nutrient medium of LEPINE *et al.* [*Ann. Inst. Pasteur*, 1956, v. 96, 654; this *Bulletin*, 1956, v. 31 (870)] was added after the culture and inoculum had been in contact for half an hour at 30°C. The reading was taken after 16 or 24 hours at 37°C.

It is claimed that by mixing antidiphtheria serum and inoculum on the one hand, Hanks solution and inoculum on the other and a control with serum alone, and transferring 0·1 ml. of each of these mixtures to a tube of tissue cultures and then proceeding as above, it is possible to establish a + diagnosis in some cases of diphtheria negative bacteriologically.

The result of this method was compared with that of direct bacteriological investigation in 248 suspect cases of diphtheria. Both methods gave negative results in 171 cases. Of 51 cases bacteriologically positive within 24 hours, 45 were positive by the technique described and the 6 others if a 24 hours broth culture of the bacterium isolated were substituted for the swab inoculum. Of 14 late bacteriological positives all gave positive results by the tissue culture method and only 5 were late positive. Finally 12 negative by the usual methods gave positives by the new method.

It is also claimed that non-specific toxic effects such as those which might arise in streptococcal or staphylococcal throat infections do not, in fact, occur.

[For a preliminary study by the authors, see this *Bulletin*, 1959, v. 34, 376.] *J. W. McLeod*

SOARE, Irina, with the collaboration of Maria GOLĂESCO, F. SPINNER, A. MARCOVICI & E. CRĂCEA. La valeur de la réaction d'agglutination pour le diagnostic de la coqueluche. [**The Value of the Agglutination Reaction for the Diagnosis of Whooping-Cough**] *Arch. Roumaines Path. Expér. et Microbiol.* 1958, Sept.–Dec., v. 17, Nos. 3/4, 523–31.

Pertussis agglutinins were found to appear during the first week of illness, reaching a maximum between the 15th and 30th days in the majority of children suffering from whooping cough. The period and clinical form of the disease, the age and constitution of the children, as well as clinical complications and antibiotic treatment, were all investigated for their effect on the appearance of agglutinins.

On the average, agglutinin titres were higher in children 3–6 years old than in those under 3. Healthy children responded better than those undernourished or rachitic, in whom the antibody response was delayed and did not reach a maximum until after the 4th week. The highest percentage of responders as well as the highest titres occurred in the children with severe clinical forms, and pulmonary complications enhanced the antibody response. Treatment with chloramphenicol had no effect on the appearance of agglutinins.

The authors conclude that detection of agglutinins is a valuable means of diagnosis during the early stages of the disease, when it confirms the bacteriological diagnosis. This is especially valuable after the second week of the disease, when the bacteriological isolations are less positive, whereas the agglutinin levels are rising rapidly. Serological tests should complement the bacteriological isolations in the diagnosis of whooping cough. *F. T. Perkins*

SPILLER, Violet & HOLT, L B. **Whooping-Cough Immunization. Clinical Follow-Up of First Barking Field Trial, 1955.** *Brit. Med. J.* 1959, Aug. 15, 174–5.

The authors and their colleagues have already reported on the 1955 field trial of whooping cough immunization in Barking [SPILLER *et al.* this *Bulletin*, 1956, v. 31, 363] and the present paper sets out the promised results of "following up" the immunized children. In the trial one group of children were given 3 injections of 1 ml. of diphtheria-pertussis prophylactic WPD (red) Wright-Fleming at monthly intervals (*i.e.*, combined method) while another group of children were given 3 injections of 1 ml. of suspended whooping cough vaccine (Glaxo) followed by 2 injections of 0·5 ml. PTAP. Injections were started when the infants were aged 2–5 months. Blood specimens were obtained from 160 of the 714 children involved when they were 15 months old and recently (4–4½ years after initial immunization) blood specimens have been obtained from 52 of the 160.

Of the original 714 children 650 (335 immunized by the combined method and 315 by the separate method) were successfully followed up in spite of the fact that as many as 300 children changed their addresses at least once. Of the 650 followed up, 22 (3·4%) "almost certainly had whooping cough" and 11 (1·7%) were reported

as doubtful. This results in a maximum rate of 5·1%. Although 8 of the "almost certain" and 4 of the doubtful cases were inoculated by the separate method compared with 14 and 7 respectively by the combined method, the probability of this difference occurring by chance was 0·1 and conventionally, at P=0·05, would not be regarded as significant. Among the 22 "almost certain" cases were 4 who had severe attacks; 2 of these had nearly a three months interval between successive injections and they developed the disease at 5 and 12 months after their last injection, whereas the other 2 were attacked at 30 and 35 months after their last injection. Only 10 of the 33 attacked children provided blood samples at 15 months—their pertussis agglutination titres ranged from 1/20 to 1/1,280.

During a poliomyelitis season there was an interruption in the immunization programme so that intervals between successive injections did exceed one month in a number of children. Such "gaps" occurred in the immunization of 9·7% of the 617 children who were not subsequently attacked compared with 24% of the 33 who were attacked.

The parents of 35 children reported home-contacts of their child with one suffering from whooping cough, but none of these children were subsequently attacked. Contacts for the 22 "almost certain" and 11 "doubtful" cases were not traced.

In view of these results the authors recommend a booster dose at the age of 15–18 months because 22 of the 33 children were attacked some 19 months after initial immunization. They also suggest that first injections might be given at 2 months as in their series these appeared to be as well protected as those who received their first injections at 3–5 months. [No data are, in fact, shown in support of this suggestion; only the average ages of first injection are given, 3·7 months for those attacked compared with 3·9 for the complete series.]

E. A. Cheeseman

MacQueen, I. A. G. & Seiler, H. E. **Report on a Comparative Test of Pertussis Vaccines.** *Med. Officer.* 1960, Jan. 22, v. 103, No. 4, 43–5.

This is a report by the Medical Officer of Health, City of Aberdeen, and the Medical Officer of Health, City of Edinburgh, on field trials undertaken in Scotland to compare the protective effect of pertussis vaccine given separately with that of combined diphtheria-tetanus-pertussis prophylactic. The average age of the children was about 7 months. One half received 3 injections of 1 ml. plain pertussis vaccine at monthly intervals followed by 2 injections of 0·5 ml. diphtheria-tetanus toxoid adsorbed on aluminium hydroxide. The other half received 3 injections of 1 ml. diphtheria-tetanus-pertussis combined antigen at monthly intervals. The period of observation was initially set at two years and subsequently extended to a total of 4 years although the actual period, as a maximum, was rather less than this.

The conclusions reached at the end of the trial was that, under the conditions obtaining, there was no evidence to show that the protection against whooping cough afforded by injecting pertussis vaccine separately was significantly different from that afforded by the triple antigen.

It is stated in the introduction to this report that the trial was a logical extension of the Medical Research Council Committee's trial in Battersea and Wandsworth where diphtheria-pertussis combined antigen was being tested [this *Bulletin*, 1959, v. 34, 985], but exactly how closely the Medical Research Council Committee was concerned in the trial reported here is not quite clear.

H. J. Bensted

Bowie, M. D. **The Management of Gastro-Enteritis with Dehydration in Out-Patients.** *South African Med. J.* 1960, Apr. 23, v. 34, No. 17, 344–8, 5 figs. [12 refs.]

In South Africa 49 out of every 1,000 children born alive to non-European parents die of gastro-enteritis between the ages of 3 months and 2 years, the comparable figure for European children being 1. This high mortality from infant gastro-enteritis has not declined *pari passu* with the general reduction in the non-European infant mortality rate; it has, in fact, slightly increased in recent years. Since hospital beds can only be made available for a fraction of the children so affected, the great majority have to be managed as out-patients after a period of resuscitation by parenteral therapy to restore the fluid and electrolyte balance [this *Bulletin*, 1957, v. 32, 415, 838, *ter*]. This paper records experience gained in the treatment of 1,185 cases during a 6-months' period in the Red Cross War Memorial Children's Hospital in Cape Town. Since the parents of 161 children defaulted before recovery was complete, only 1,024 case-histories are analysed. Of these, 923 concerned children treated solely as out-patients.

The disease shows marked seasonal variation being commonest in the summer months of December–April, with peak incidences in February–March. The age-group most affected is that between 2–6 months, the greatest numbers being 3–4 months old. After 2 years of age, only sporadic cases of gastro-enteritis with dehydration occur. Malnutrition is a potent factor predisposing to death from this disease, the weight of children dying of gastro-enteritis, prior to the onset of the disease being only 12 lb. at 1 year, as compared with the still very poor mean weight of 13 lb. 8 oz. of the non-European child not so affected, and the lowest American figure of 18 lb. 8 oz.

A standard treatment of gastro-enteritis has been adopted in this hospital [*ibid.*, 1957, v. 32, 838]. When clinical signs of dehydration are absent all feeds are stopped and the child is put on half strength Darrow's solution in 2½% dextrose water by mouth in frequent drinks totalling 3–4 oz. per lb. weight in 24 hours. After this time unless vomiting persists, full strength feeds of skimmed- or whole-cream milk are resumed. [This prompt resumption of full-strength feeds, though unconventional, is prompted by the concomitant malnutrition: it appears to work well.] Anti-bacterial therapy is also given in the form of an injection of a long-acting penicillin and a soluble oral sulphonamide for 5 days. Should these prove ineffective oral chloramphenicol is substituted. This agent is used initially for those patients who present with frank dysenteric symptoms.

Parenteral fluid administration is indicated in those

showing clinical signs of dehydration, acidosis, peripheral circulatory failure or severe vomiting. In mildly dehydrated children subcutaneous infusion is used in amounts estimated by the weight deficiency, usually amounting to 10% of the body weight. Half-strength Darrow's solution in 2½% dextrose is usually employed, an alternative is to give half the required amount as half-normal saline in 2½% dextrose solution, followed by half-strength Darrow's solution. Hyaluronidase is used to aid diffusion.

In severely dehydrated, acidotic infants intravenous infusions are given comprising half-strength Darrow's solution in 2½% dextrose water in amounts sufficient to supply the replacement and maintenance fluids. The replacement fluid is calculated as 10% of the body weight and the total amount administered in 24 hours amounts usually to 50 ml. per lb. body weight replacement fluid and 80 ml. per lb. maintenance fluid, a total of 130 ml. per lb. A scalp or arm vein is usually used, cutting-down being seldom necessary. Small oral feeds of the same solution are also given.

This parenteral therapy is given in a special resuscitation room, and the mother waits with the baby until the infusion is complete, returning with the child to hospital next day for re-examination.

Most infants recovered within 3–4 days of re-hydration, though 17% required further infusions. The total mortality of children suffering from acute gastro-enteritis with dehydration was 9·5% but this included 29 deaths among the most severely affected who were admitted to the wards. The mortality of these treated solely as outpatients was 7·4%. [This seems an eminently practical and successful approach to this very grave problem.]

J. H. Walters

BOLDYREV, T. E., ALEKSANIAN, A. B., SHATROV, I. I., KORSHAKOVA, A. S., LEITMAN, M. Z., FROLOV, V. I. & KOVALEVA, N. I. **A Study of the Efficacy of Dysentery Alcohol Vaccine in Large-Scale Epidemiological Experience.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 7, 1–5. [Translated from Russian.]

This paper describes a well conducted controlled field trial of a Flexner-Sonne alcoholized dysentery vaccine. The trials were carried out in three areas in which a total of some 34,000 persons aged 15–51 years and over were investigated, the majority of whom were in the 21–40 year age-group. The only selection of the participants was that none should have been vaccinated against dysentery within 2 years and that all should be exposed to approximately the same sanitary, industrial and epidemiological conditions. Throughout, the participants—18,000 vaccinated and 16,000 unvaccinated—were observed by groups of trained epidemiologists. Sera from a number of inoculated subjects were used in the mouse passive protection test and the results indicated that the vaccine induced the development of protective antibodies but that the protection was short lived. The clinical and epidemiological studies over a period of 5 months from the time the trial started failed, however, to show that the vaccine had any influence on the incidence of Flexner or Sonne dysentery. Indeed, the actual numbers of persons who became infected were slightly higher (1·4%) in the vaccinated group than in the non-vaccinated.

H J. Bensted

DEVOINO, L. V. **Studies of Immunological Changes against Dysentery Antigens in Persons inoculated with Chemical Combined Adsorbed Polyvalent Vaccine Depot produced by the Gamaleya Institute of Epidemiology and Microbiology.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 7, 10–15. [16 refs.] [Translated from Russian.]

The author does not disclose exactly what this "Polyvalent Vaccine Depot" is, but indicates that it represents the "complete phenol antigens" of *Salmonella typhi, Salm. paratyphi B, Shigella flexneri* types *c* and *f* (common types in U.S.S.R. nomenclature) and *Sh. sonnei* together with the tetanus toxoid. The paper is concerned only with the immune response to the shigella fractions, which gave significant agglutinin titres against Flexner, but none to *Sh. sonnei.* An increase in the phagocytic power was also observed and this appeared to continue at about the same level for about 4 months after which it declined. There was some increase in the protective power of the sera of inoculated persons against Flexner infections as judged by the mouse passive protection test. [This is not a very helpful paper.]

H. J. Bensted

LEWIS, J. S. **Brucellosis in Krugersdorp, with a Review of the Problem in Southern Africa.** *South African Med. J.* 1959, Feb. 28, v. 33, No. 9, 177–81. [17 refs.]

The author gives brief notes of 10 cases of brucellosis diagnosed in Krugersdorp in the Transvaal and a general review. No new aspects of this disease are recorded but the author shares the often repeated view that many cases are still undiagnosed.

Frederick J. Wright

MATHUR, T. N. **Brucellosis simulating a Respiratory Illness. A Report of Eleven Cases.** *Indian J. Med. Sci.* 1960, July, v. 14, No. 7, 610–18. [26 refs.]

Pulmonary symptoms and signs have frequently been reported in brucellosis but delays in diagnosis continue to occur through a failure to test for sero-agglutinins in patients with fever and cough. The author gives the case records of 11 such patients in whom diagnoses of pneumonia, bronchitis, pulmonary tuberculosis, influenza, bronchopneumonia or dry pleurisy were initially made. Response to chloramphenicol may lead to a mistaken diagnosis of typhoid fever. In 3 of the 11 cases *Brucella melitensis* was cultured from the blood. Sero-agglutinins were present in all, usually in high dilution.

The author reviews the literature and refers to the granulomatous lesions resembling carcinoma described by WEED *et al.* [this *Bulletin*, 1952, v. 27, 655, and 1956, v. 31, 1101] and RAMAH *et al.* [*ibid.*, 1959, v. 34, 1248].

[A useful reminder. The granulomatous lesions described by Weed and Ramah were due to *Brucella suis.*]

Frederick J. Wright

TAPIE, J., MONNIER, J., FREJEVU, Y., MOLE, & ANDRÉ, J. Phlegmon périnéphrétique d'origine brucellienne. [**Perinephric Abscess of Brucellar Origin**] *Bull. Acad. Nat. Méd.* 1960, v. 144, Nos. 19/20, 388–94.

The authors report on a patient suffering from recurrent fever where the diagnosis was obscure until a perinephric abscess was treated surgically and the pus yielded *Brucella melitensis* on culture. Although lesions in the genito-urinary tract due to *Brucella* are well known, the authors have been unable to find a record of a previous perinephric abscess due to *Brucella* and, in this case, there was no evidence of bacterial endocarditis or prolonged bacteriaemia. The subject was a butcher who, in 1956, had had a febrile illness in which the diagnosis of brucellosis was supported by sero-agglutinins in a dilution greater than 1 in 60. The patient refused antibiotics. Brief spells of fever recurred 5 months later but the serum had become negative and remained so. There was a slight leucocytosis but the percentage of neutrophils was within normal limits. The sedimentation rate was 40 mm. in 1 hour. Temporary relief only was obtained from antibiotics and steroid therapy.

Eventually, nearly 2 years later, the patient agreed to investigation in hospital and radiography showed an immobile right diaphragm with flattening of the contour posteriorly, and pyelography showed a displaced renal pelvis. There was only slight tenderness in the loin. At operation, although a perinephric abscess was encountered, the right kidney was with difficulty removed as the appearances were suggestive of malignancy. After a stormy convalescence, attributed to suprarenal inefficiency, the patient made a full recovery. Pathological examination showed the kidney to be unaffected.

Frederick J. Wright

FOGEL, R. & LEWIS, S. **Diagnosis of *Brucella melitensis* Infection by Percutaneous Needle Biopsy of the Liver.** *Ann. Intern. Med.* 1960, July, v. 53, No. 1, 204–6.

The patient was a butcher who had sustained an abrasion of the forearm from a jagged piece of hog bone 2 weeks before the onset of fever. He was found to have a palpable, firm, non-tender liver. There was a relative lymphocytosis and sero-agglutinins to *Brucella* were present in a titre of over 1 in 640. 7 blood cultures were negative. A liver biopsy yielded *Brucella melitensis* on culture after 5 weeks. Successful treatment with chlortetracycline was begun immediately after the biopsy. The infection is presumed to have been porcine although the species was *melitensis*.

Brucella abortus has been obtained from liver biopsy when blood cultures have been negative, by MCCULLOUGH and EISELE [*Arch. Intern. Med.*, 1951, v. 88, 793; this *Bulletin*, 1952, v. 27, (427)] and COHEN *et al.* [*ibid.*, 1957, v. 32, 1150], and *Br. suis* by WAGONER *et al.* (*Gastroenterology*, 1953, v. 25, 487) but the authors know of no previous record of *Br. melitensis* obtained in this way.

[BRUCE obtained the organism, presumably *Br. melitensis*, from the spleen in life in 1891.]

Frederick J. Wright

OLITZKI, A. L. [**Immunization of Men by Living Attenuated Brucellae**] *Harefuah.* Jerusalem. 1960, July 15, v. 59, No. 2, [in Hebrew 37–8. English summary 38].

The English summary appended to the paper is as follows:—

"A preliminary experiment was performed in order to determine whether it is possible to immunize man against brucellae orally. An adult volunteer received living non-virulent brucellae *per os*. First *Br. abortus* 19D and later *Br. melitensis* Rev. I were employed. A rise of the agglutinin titer was observed when more than 100 millions of the latter strain were administered. No clinical symptoms of an infection were observed."

SKRODZKI, E. **Investigations on the Pathogenesis of Tularemia. Report II. On the Phagocytic Role of Leukocytes in *B. tularense* Infection.** *Bull. Inst. Marine Med. Gdańsk.* 1960, v. 11, Nos. 1/2, 35–46, 5 charts.

"On the basis of the results obtained the following data were established:

"1. A faint leukocytic response of the peritoneum after its infection with *B. tularense*.

"2. *B. tularense* exerts a slight chemotactic influence on leukocytes.

"3. *B. tularense* phagocytized by leukocytes remain for more than 24 hours alive.

"4. It was not possible to prove the protective role of leukocytes in tularemia exactly."

SNEDDON, I. B. **Accidental Acquired Hypersensitivity to Tetanus Antitoxin.** *Brit. Med. J.* 1960, May 14, 1468–9.

A full account is given of a case of allergic reaction to tetanus antitoxin in a young medical graduate. Suspicion that oedema of her eyelids, which had appeared after this young woman had been administering antiserum to patients, was due to access of droplets of serum to her eyes had arisen. An intradermal injection of 0·2 ml. of a 1 in 10 dilution of the serum was given to test this hypothesis. The reaction was startling, a local weal was rapidly followed by bronchospasm, vomiting and generalized urticaria. She continued to exhibit very severe and menacing symptoms for 4 days and was not discharged from hospital till a week had passed. Antihistamine and cortisone treatment was used freely but did not appear to give much relief. After 24 hours of illness she received phenobarbitone and appeared to respond better to this than to the other drugs. Although there was no clear suggestion of allergy in the patient's history, it would undoubtedly have been better to use a 1 in 100 dilution of serum in the test dose. The obvious advantage of active immunity is underlined.

J. W. McLeod

STAFFORD, E. S. **Active and Passive Antitetanus Immunization.** *J. Amer. Med. Ass.* 1960, June 4, v. 173, No. 5, 539–41.

This is a well balanced up-to-date lecture on the prevention of tetanus and is essentially practical in nature. It does not offer any new information but gives adequate consideration to the prophylaxis of tetanus by other means before dealing with active and passive immunization as a problem in civilian medicine in the United States. While it may be said to be a plea for mass inoculation of the population with tetanus toxoid the lecture devotes considerable space to passive immunization as an immediate problem. It is not known whether the population of the United States is, in general, more sensitive to horse protein than the population of Great Britain, but the author suggests that hypersensitivity is such a hazard that the physician's main problem is often to decide whether the danger to life is greater from tetanus or from the effects of the horse serum. In this connexion he considers the possibilities of human immune serum for passive immunization. Combined active and passive immunization in tetanus is a difficult problem in the critical 5–6 day period in tetanus-prone injuries and perhaps the author is wise to skate over this, for at present there seems to be no very satisfactory answer, but he does give consideration to the value of penicillin and the broad-spectrum antibiotics for immediate therapy as a means of reducing toxin formation by preventing the growth of tetanus bacilli. This is a very well prepared lecture and worthy of study. *H. J. Bensted*

MITOV, A., YANKOV, N. & IVANOV, I. Recherches sur le problème des reservoirs des leptospires dans les terrains de rizières. [**Studies on the Problem of Reservoirs of Leptospires in Rice-Fields**] *Folia Med.* Plovdiv. 1960, v. 2, No. 1, 21–4.

In Bulgaria, leptospiral infections occur in nearly every part of the country; but the highest incidence of cases and the widest variety of types [? clinical, ? serological] are found in the rice-fields of the Maritza river basin, especially in the department of Plovdiv. The commonest serotypes of *Leptospira* are *bataviae*, plovdiv (=*mini*) and nicolaevo (Autumnalis group). In addition, *L. pomona* is known to cause sporadic cases and limited outbreaks of infection: the latter have been found to be related to piggeries situated near water and up-stream from the places where human infections were apparently contracted.

In the past, *L. bataviae* was isolated from *Apodemus agrarius* and *Micromys minutus*, and *L. icterohaemorrhagiae* from *Rattus norvegicus*. During the last few years the authors have made a special study of the rodents inhabiting the rice-fields of Plovdiv: their findings are reported in the present paper. Emulsions of kidney were examined microscopically and by culture in Terskich's medium.

In 1958, leptospires were isolated from 9 out of 112 *M. minutus*, a low incidence because the animals were young: of these strains, 5 were identified (*L. bataviae*).

In the following year, 33 strains were isolated from 177 rodents: *Arvicola terrestris*, 8 out of 51 (*L. pomona*, 1; *L. mini*, 7); *Microtus arvalis*, 9 out of 47 (*L. pomona*, 4; *L. mini*, 3; *L. australis A*, 2); *Micromys minutus*, 14 out of 71 (*L. pomona*, 2; *L. mini*, 2; *L. bataviae*, 10). *Mus musculus* (7) and 1 rat proved negative. [There are some minor discrepancies in the text and 2 strains are not mentioned.]

Of particular interest is the establishment of 3 rodent carriers of *L. mini*, a serotype which has not been studied very much. *L. H. Turner*

AKTAN, M. **A Serological Investigation on Leptospira Infections in the Three Southern Provinces of Turkey.** *Türk Ijiyen ve Tecrübî Dergisi.* Ankara. 1960, v. 20, No. 1, 101–3. [Fuller version in Turkish 97–9. (15 refs.)]

"Of the 700 sera collected from the rice-fields workers in the three southern provinces (Adana, Hatay, Maras) of Turkey in June 1959, 91 (13%) sera were found positive in the agglutination-lysis test carried out with ten different Leptospira antigen. It was concluded from this experiment that the agent of this endemic is mainly L. grippo-typhosa (89%), and then L. icterohaemorrhagiae (5·5%) and L. bovis (5·5%)."

WOOD, G. E. & ALEXANDER, A. D. **The Effect of Selected Antibacterial and Antiprotozoal Agents in Treatment of Leptospirosis in Experimentally Infected Hamsters.** *Antibiotics & Chemotherapy.* New York. 1960, June, v. 10, No. 6, 341–8. [21 refs.]

This paper is from the Department of Veterinary Bacteriology, Walter Reed Army Medical Center, Washington. Hamsters were inoculated intraperitoneally with *Leptospira canicola* in numbers killing all controls in 6–11 days. Treatment with pentamidine, nitrofurantoin, chloroquine, and the dimercaptosuccinates of antimony and arsenic was without effect. Kanamycin had a slight and inconstant effect. Oleandomycin in a dose of 25 mgm./kgm. daily saved all the animals if given on the 3rd or 4th day after inoculation and some if given later; in 4 times this dose it saved all animals even if given as late as the 7th day, and also regularly abolished "leptospiruria", which the lower dose did not. It is pointed out that other serotypes of leptospira may differ in their sensitivity to this antibiotic. [These findings would have gained in possible therapeutic significance if a comparison had been made with antibiotics of which the action in leptospirosis has already been well studied, particularly penicillin, tetracyclines and erythromycin.]

L. P. Garrod

DEL NEGRO, G. & YABUTA, D. Emprêgo de um novo antibiótico (demetilclortetraciclina) na moléstia de Weil. Resultados preliminares. [**The Use of a New Antibiotic (Demethylchlortetracycline) in Weil's Disease. Preliminary Results**] *Rev. Inst. Med. Trop. São Paulo.* 1960, May–June, v. 2, No. 3, 140–46. [20 refs.]

The English summary appended to the paper is as follows:—

"Four patients with Weil's disease were treated with a new broad spectrum antibiotic belonging to the tetracycline group—the 7-chloro-6-demethylchlortetracycline. This new antibiotic was obtained from a mutant strain of *Streptomyces aureofaciens* Duggar in 1957, at the Lederle Laboratories in New York.

"The clinical diagnosis of Weil's disease in the four patients was confirmed by positive agglutination test for *Leptospira icterohemorrhagiae* in titers equal to or above 1 : 400. The total dosage range of the antibiotic was 4.2 to 8.1 grams. The four patients improved quickly; no second week febrile period appeared in any patient; complications did not occur; no side effects were noticed, and all four patients were discharged in good health."

VIRUS INFECTIONS

The order in this section is:—*General, Psittacosis-Lymphogranuloma group, Pox group, Respiratory group, Reovirus group, Enteric group, Arthropod-borne group, Others.*

MEYER, K. F. & EDDIE, B. **Feather Mites and Ornithosis.** *Science.* 1960, July 29, v. 132, 300.

This is a brief note recording the most interesting demonstration of ornithosis virus in ectoparasites of poultry. In one instance the infected insects came from a chicken flock in which there was serological evidence of infection but a complete absence of clinical ornithosis for a period of 3 years. In a second case the insects were collected on a turkey farm on which ornithosis had been occurring annually. These insects, from which ornithosis virus was again isolated by mouse inoculation, were collected from nests which had had no turkey occupants for 2½ months. *S. P. Bedson*

HOBDAY, T. L. **New Views on Protection against Smallpox.** *J. Roy. Army Med. Corps.* 1960, July, v. 106, No. 3, 103–6.

The "new views" concern the use of hyper-immune anti-vaccinial gamma globulin in unprotected smallpox contacts; and a plea for a vaccination technique in the face of smallpox which is bolder than that employed routinely. [This has been standard practice in England almost since the introduction of "one mark" vaccination.] Reference is made to the work of CROSS [this *Bulletin*, 1959, v. 34, 1075] which suggests that the development of immunity is more speedy when the vesicle is substantial.

[The proper place of gamma globulin in the protection of smallpox contacts has still to be determined and, in the opinion of the abstracter, articles which may give the uninitiated reader the impression that the complete answer lies in the use of gamma globulin can be highly dangerous. English experience—here incompletely quoted—has been far too small to be of any significance. Experience from India has been vitiated by lack of accurate information on the vaccinal state of those concerned. Successful vaccination remains the sheet anchor of protection against smallpox, and nothing should be done to minimize the importance of a good take. Incidentally, it is depressing to find once again the same old misinterpretation of Ricketts on vaccination after exposure, attention to which has been drawn by the abstracter so many times.] *J. Pickford Marsden*

LIPPI, M., BENEDETTO, A. & FRUGONI, G. Contributo sieroimmunologico alla conoscenza delle principali virosi. Ricerca nei soggetti sani degli anticorpi devanti il complemento verso l'antigene comune de gruppo degli adenovirus. **[Study of Complement Fixing Antibodies to the Adenovirus Group in Healthy Subjects]** *Arch. Ital. Sci. Med. Trop. e Parassit.* 1960, Aug., v. 41, No. 8, 397–412. [74 refs.]

The English summary appended to the paper is as follows:—

"The authors have studied the diffusion of antibodies fixing the complement for the antigen of the Adenoviruses group in 537 sera coming from three different groups of individuals:

"The first group concerns 403 healthy individuals of ages ranging from 1 month up to more than 60 years, living in Rome, not belonging to any close community.

"The second group concerns 75 healthy adult individuals of ages ranging from 18 to 58 years belonging to an agricultural community in the area of Rome.

"The third group concerns 59 individuals of ages ranging from 13 months to 12 years, from a hospital service in the province of Rome, suffering from tubercular diseases.

"The authors have put in evidence a rate of antibodies fixing the complement for the Adenoviruses in 18.3% of the subjects of the 1st group, in 25.2% of the subjects of the 2nd group and in 35.6% of those of the 3rd group."

PIERCE, Cynthia H. & KNOX, Alice W. **Ciliocytophthoria in Sputum from Patients with Adenovirus Infections.** *Proc. Soc. Exper. Biol. & Med.* 1960, July, v. 104, No. 3, 492–5, 7 figs. [10 refs.]

In previous studies the sputa of persons suffering from acute respiratory tract infections were stained with PAPANICOLAOU'S stain (*New York State J. of Med.*, 1956, v. 56, 2647) and in certain cases degenerating ciliated epithelial cells were detected. These cells showed inclusions and other abnormalities, called collectively ciliocytophthoria (CCP), and were found only in cases of influenzal or "probable viral" aetiology.

This paper reports a study of sputa from 282 recruits suffering from acute respiratory disease during a period when 77% of such cases showed serological evidence of adenovirus infection. 59% of specimens showed typical CCP and 11% were abnormal to some extent. Sera from 32 patients, of whom 27 showed CCP, were tested against adenovirus and influenza A antigens. 22 sera showed significant antibody rises against adenovirus alone, and

3 showed rises against influenza A alone. The sera from 5 patients with negative cytology were all positive for adenovirus.

It was not possible to distinguish in the Papanicolaou-stained preparations between the effects of adenovirus infection and those of influenza virus infection.

D. A. J. Tyrrell

SPICER, C. C. **Influence of some Meteorological Factors in the Incidence of Poliomyelitis.** *Brit. J. Preventive & Social Med.* 1959, July, v. 13, No. 3, 139–44, 1 fig.

An analysis is made of the monthly variation in poliomyelitis incidence and 3 meteorological variables in England and Wales from January 1947 to December 1956. The smallest unit of time considered was a calendar month and for each of the 120 resultant months the 4 relevant variables are tabulated; they are, P = mean weekly logarithm to base 10 of the number of uncorrected notifications of poliomyelitis published by the Registrar General, T = mean dry bulb temperature in °F, VP = mean vapour pressure in millibars and RH = mean relative humidity. The variables T and VP were monthly averages of 4 daily readings taken at London Airport, Plymouth, Tynemouth and Manchester from Meteorological Office records for most of the period, although for 1947–50 data available from a previous enquiry were used. RH was estimated from a graph of the relationship between saturation vapour pressure and temperature.

The main analysis consisted of an examination of the residuals of the 4 variables after the seasonal (monthly) and long term (years) trends had been removed by the analysis of variance method of fitting constants. Multiple regression analysis of the residuals of P on those of T and RH in the same and earlier months showed that 36% of the variation in the poliomyelitis residuals could be accounted for by their association with temperature and relative humidity in the same and the two preceding months. The correlations of P with T residuals were strong and positive and P with RH residuals were negative. The VP residuals were not considered because preliminary investigation showed them to be of little importance. Similarly unimportant were the effects of T and RH residuals of more than two months before the month of the P residual being predicted.

The resultant regression equation is shown to account reasonably well for the average seasonal variation in poliomyelitis incidence over the 10-year period and indeed the discrepancies which do exist could be explained by undernotification in the early stages and overnotification in the late stages of the epidemic period. The statistical methods used in this paper are critically examined by the author and possible hypotheses resulting from this analysis are formulated. Thus "A possible hypothesis is that atmospheric conditions of rapid drying favour survival of the virus in faeces, and one suggestion that arises from the present study is that this should be put to experimental test."

[See also this *Bulletin*, 1951, v. 26, 211; 1953, v. 28, 402.] *E. A. Cheeseman*

HOLT, L. B. **A Re-Assessment of the Risk of provoking Paralytic Poliomyelitis by making Prophylactic Inoculation against Diphtheria and Pertussis.** *J. Hygiene.* 1959, June, v. 57, No. 2, 150–61. [16 refs.]

In 1956 the Medical Research Council (MRC) examined the evidence then available about the provocation of paralytic symptoms by diphtheria, whooping cough and smallpox immunization procedures, in patients infected by poliomyelitis viruses [this *Bulletin*, 1957, v. 32, 233]. Investigations were based on data relating to poliomyelitis in England and Wales in 2 periods, 1951–53 and 1954–55. In the present paper these data were re-examined and "it is concluded that the use of combined diphtheria fluid toxoid and pertussis vaccine, administered in early infancy, incurs a minimal risk and is to be recommended because of its immunological efficiency, its unquestionable value in helping to maintain a high immunization rate against diphtheria in the child community and for its marked administrative convenience".

The number of cases of paralytic poliomyelitis following the inoculation of a number of children with a given prophylactic can be theoretically expressed as the product of three quantities: (1) N = number of "child-inoculations", (2) P = probability of a child being infected with a poliomyelitis virus at the time of inoculation and (3) R = the "provocation index". For this purpose N is taken as one injection and time for resultant exposure is limited to 28 days. R can be defined as the number of children with a latent poliovirus infection who develop paralysis within 28 days of an injection compared with an identical uninoculated population in which only one case of paralysis occurs. In the notation of this paper the total number of cases of paralytic poliomyelitis in any group of inoculated children is (S+I+D) where S = the number of children with paralysis only in the same body site as the injection (same site), I = the number with paralysis in the same and other body sites as the injection (included sites) and D = the number with paralysis in a body site other than that of the injection (different sites).

An overall estimate of R was made for all arm and leg inoculations involving 7 prophylactics, for each period separately, by considering paralytic cases in the 29–84 days after inoculation as control data (*i.e.*, paralysis occurring more than 28 days after an injection was considered unlikely to be provoked by that injection) and calculating R as (i) (S+I) in 1–28 days after injection divided by the 4-week average of (S+I) in 29–84 days after injection, and (ii) as before but using (S+I+D) in place of (S+I). The estimates for R were: 1951–53, (i) 5·29, (ii) 1·96; and 1954–55, (1) 1·52, (ii) 0·95. It is pointed out that the estimates (i) are the more acceptable on the hypothesis that the paralysis-provoking effect of an injection is anatomically related to the inoculation site.

Accepting such a hypothesis permits another approach with the use of the D cases of paralysis as controls. Considering only paralytic cases in 29–84 days after inoculation, values for K = D/(S+I) were calculated as 3·3 for 1951–53 and 3·25 for 1954–55. In the absence of provocation paralysis K(S+I)/D is expected to be unity so that with the data relating to 1–28 days after injection

$R=K(S+I)/D$, where K is reasonably taken as 3·3. A variation of this approach is possible if the I cases are omitted so that $R'=K'S/D$ where $K'=9$ is shown to be reasonable.

Estimates of R and R′ from 1951–53 and 1954–55 data combined (and separately where numbers are sufficient) are tabulated for arm inoculations for APT, PTAP, TAF and FT, pertussis vaccine, mixed with alum (1951–53 only) and mixed without alum. The original MRC estimates adjusted for comparison are also shown for 1951–53. The estimates from the 1–28 day data showing in order MRC, R and R′ were APT, 2·64, 4·62, 7·2; PTAP, 4·6, 3·3, 6·75; TAF and FT, 1·075, 1·65, 3·0; pertussis vaccine, 1·46, 4·125, 4·5; mixed with alum, 6·15, 21·4, 54·0; mixed without alum, 5·0, 3·3, 6·2. For all prophylactics combined $R=4·5$ and $R'=8·0$. Where it was possible to make estimates for each period separately, it was found that they were lower in the second period, implying a reduction in provocation. Some investigation of this reduction is made and as a result the possibility that provocation is more closely allied to Type 2 than other poliovirus types requires further investigation. However, the main interest in the above estimates lies in the fact that those by the MRC for pertussis vaccine alone are small and those for vaccine plus toxoid are large, whereas in contrast the new estimates for the vaccine alone are large and not very much different from those for vaccine plus fluid toxoid.

[On pages 154 and 155 of this report formulae and calculations are frequently stated ambiguously, *e.g.*, $R=S+I/D\times 3·3$ should be $3·3(S+I)/D$ and $43/28\times 3·3=5·06$ is better written $3·3(43/28)$.] *E. A. Cheeseman*

CHASSAGNE, P. & GAIGNOUX, Y. Caractères épidémiologiques de la poliomyélite en France en 1958. **[Epidemiological Features of Poliomyelitis in France in 1958]** *Bull. Inst. Nat. Hyg.* Paris. 1960, May–June, v. 15, No. 3, 491–515

In 1958 the Institut National d'Hygiène received 837 epidemiological reports on patients in France who had acute anterior poliomyelitis. An analysis of these reports is presented in a series of tables amplified by text comments following the plan used in previous years. The distribution of the cases is given in terms of a number of factors of epidemiological interest; these include type of onset, presence of meningeal signs, anatomical site and extent of paralysis, survival and type of residual disability, treatment, possible source of infection, urban and rural dwelling and time of year. These distributions are usually shown for specified age and sex groups and two-way classifications of the distributions of some factors are given. Comparisons with previous years are shown.

[Unfortunately the reports were not complete in all respects, and as a result, in many of the tables the number of patients for whom information was not available was quite large. These omissions, coupled with the fact that there were in all 1,647 cases notified in France in 1958, make the interpretation of the tables very difficult, consequently no numerical details are given in this abstract.] *E. A. Cheeseman*

LINDAHL, A. **The Poliomyelitis Outbreak in Copenhagen in 1952. Epidemiological Studies.** *Acta Med. Scandinavica.* 1960, v. 167, Suppl. 355, 167 pp., 2 charts & 1 fig. [Numerous refs.]

This report describes a comparison made between a random sample of the patients with acute anterior poliomyelitis admitted to the Blegdamshospitalet during the 1952 epidemic in Greater Copenhagen and a sample of the population of that town matched for age and place of residence with the admitted patients, but otherwise drawn at random. The main factors which were compared included frequency of contact with known cases of the disease, composition of the subjects' households, social and sanitary conditions under which the subjects were living and their activities, associates and next of kin. A chapter is devoted to a number of factors thought to influence the clinical course of the disease.

The population of patients from which the sample was drawn was restricted to admissions from a defined area of the city between July 15 and December 31, 1952. It consisted of 2,247 patients who fell into one of 3 diagnostic groups: (1) paralytic acute anterior poliomyelitis, (2) non-paralytic acute anterior poliomyelitis with morbid changes in spinal fluid, (3) abortive acute anterior poliomyelitis without paralysis or spinal fluid changes. There were a further 370 patients who could have been members of the last group but they were excluded from the population sampled because the following criteria were not satisfied: (1) presence of meningeal signs, (2) raised temperature, (3) other causes of fever excluded by investigation and (4) disease not treated by chemotherapy or antibiotics. A sample of 316 patients was drawn at random from this population and a control sample matched for age and place of domicile was obtained by otherwise random sampling of first the households in the area and then the subjects within the households. Visits were made to the patients' and controls' homes (patients were also seen in hospital) and a comprehensive questionnaire was completed by interview with subjects, parents and other relatives. The analysis of replies are presented in a series of simple tables showing results for each sample as a whole and each broken down into two age-groups—children (*i.e.*, under 15 years) and adults.

The patients appeared to have more frequent contact with persons who had signs and symptoms than did the controls. Thus 28·2% of the patients in the sample were known to have had contact in the 20 days preceding onset of disease with an admitted patient compared with 4·1% of the controls in a corresponding 28-day period. However, none of the contacts experienced by the sample members with admitted persons were with members of their own families. The number of persons in the 316 households of patients was some 20% greater than that in controls' households; there were, however, 24 cases from patients' households compared with only 3 from controls' who were admitted in the 20 days after onset of disease in the propositi or corresponding date in the controls.

There were relatively more children in the patients' than in the controls' households. There was at least one child in 90·1% of the patients' households compared with 82·0% of the controls. If this comparison is confined to adult patients and their controls, the corresponding

proportions are 65·9 and 38·7% respectively. Further analysis of the household compositions revealed that children aged 1–5 years of age were more often found in the patient than in the control households particularly when the propositi were aged 6 years or over or in the first year of life (51·6% of patients at these ages had children aged 1–5 in their households compared with 16·0% for controls). It is suggested that the most likely explanation of this and other relevant findings is that "infection with clinically manifest acute anterior poliomyelitis is more often transmitted by children of the age group 1–5 years than by all other age groups".

Subsequent analysis of the "social and sanitary status" and the "activities" of the patients and controls was almost impossible to interpret because of the basic difference in the composition of patient and control households. [The numbers were insufficient to break either sample down into sub-groups with households of similar size and probably for this reason no attempt is made to formally investigate the possible interactions of the large series of factors considered.] As it is, straightforward comparisons between patients and controls, for each environmental factor separately, did not demonstrate any significant differences. The main factors given attention were the distribution of the samples by occupation (food handling and others), work done by mother, income, type of home (own, flat, tenants, etc.), number of rooms, bedrooms and beds, lavatory and toilet facilities, interviewer's assessment of hygiene and care of homes, contact with sewage-polluted water, presence of household vermin, possession of garden, fruit eating habits, holiday arrangements, frequency of changing address, use of children's camps and public playgrounds and association with other children.

From the section dealing with factors thought to influence the clinical course of the disease the author concluded that no differences between the patient and control samples occur which cannot be explained by the contagiousness of the disease or the different composition of the households. Among the factors considered were the history of poliomyelitis in the households, the history of lymphocytic meningitis and head injury, hair and eye colour, physical activity during illness and work [these data, as presented, are particularly difficult to interpret and further consideration is required] and the frequency of vaccinations, injections, venipuncture and capillary puncture and surgery. [A comparison was also included in terms of the history of pregnancy and the time of menstruation in relation to onset of disease, but the women for whom such data were available were not shown to be of comparable age in the two groups, so that the observed results are of little value.]

From the experience of the staff working at the hospital it is concluded that the disease is not contagious after onset of symptoms. The author discusses the infection within households and states "the age distribution within the patient households militates against acquired immunity from previous infections with poliomyelitis virus being of significance in respect to the appearance of clinical symptoms. This phenomenon may best be explained as a competitive inapparent and overt infection, depending upon the age of the infecting person. Thus, part of the infections found among the household members must be assumed to have preceded that in the child who transmitted infection leading to overt disease, which in turn can manifest itself in non-infected persons and never in those already infected." Generally among adults the risk of clinical manifestation of disease appeared to be greatest in those associating with young children in a household, while the risk among pre-school children appeared to be greatest in those associating with other young children. Thus "whatever involves increased association, and thereby an increased possibility of infection, among children of pre-school age, entails a likelihood of a large number of cases of poliomyelitis, not only in this age group, but also among these children's next-of-kin. Recent years' violent outbreaks in big cities must be viewed on this background, and preventive measures ought to aim at this age group as a whole."

E. A. Cheeseman

LEVY, D. & FALK, W. **Epidemiological Study of Poliomyelitis in Northern Israel, 1950–1956.** *Amer. J. Pub. Health.* 1960, June, v. 50, No. 6, Pt. 1, 843–54.

Before 1949 poliomyelitis was very rare in Palestine. From the latter half of 1949 until 1956 there occurred an epidemic of poliomyelitis with peaks of incidence each summer. The authors have made an epidemiological study of poliomyelitis in the northern part of Israel during the epidemic years in an attempt to decide whether the epidemic was due to a new strain of virus or to changes in the immune status of the population. No virological evidence is presented but the possibility of a new strain of poliovirus is at least suggested by the increased incidence of the disease in Arabs during these years. This was confined to young children so that the adults must be considered immune to the new strain which might have been of greater virulence rather than antigenically novel.

During the epidemic period large-scale immigration into Israel occurred. This was of two main sorts, those from countries with a high social, cultural and hygienic standard and those with low standards. The proportion of those from backward countries increased during the period. Efforts were made to mix these populations to achieve an integrated political state with the incidental result of spreading viruses between the groups. It is suggested that poliovirus was prevalent among the lower group of immigrants and their children were infected early in life. Thus, 48% of the patients in the group were under 1 year and only 9% over 3 years in 1950. The children of the higher group of immigrants were not infected until later in life, as they came in contact with the lower group's children, and suffered a higher incidence. Thus 27% of the patients were under 1 year, 51% 1–3 years and 22% over 3 years in 1950. Similar figures were found in other years.

A. J. Beale

AKERS, T. G., HASHEM, N. & MAHDY, M. S. **Studies on Paralytic Poliomyelitis in Cairo, U.A.R., 1957–1958.** *Amer. J. Trop. Med. & Hyg.* 1960, May, v. 9, No. 3, 343–9, 2 figs. [21 refs.]

Since the work of PAUL *et al.* [this *Bulletin*, 1952, v. 27, 1092] it has been realized that poliovirus infections are

widespread in Cairo. However, rather little study has been made of patients with poliomyelitis who, as Paul *et al.* noted, usually do not visit the doctor in the acute stage of the illness. This valuable paper records virological studies on 830 out of 1,741 cases of paralytic poliomyelitis reporting to the Children's Hospital, Cairo, during the period July 1957 to June 1958. These 830 patients were those reporting within 15 days of onset. 86% had isolated spinal paralysis and 14% some form of polio encephalitis. 97% of the patients were under 30 months old. Viruses were isolated from rectal swabs of 60% of the cases. 447 isolates were poliovirus and 50 other enteroviruses. The poliovirus distribution was type 1, 61%, type 2, 31%, and type 3, 8%, whereas in 1955 the distribution was 38%, 43% and 19% respectively. 94% of the patients yielding a poliovirus were between 7–30 months and 38% were 7–12 months. 60% were males. The virus isolations were equally prevalent all year round. The attack rate in the 0–4 year age-group was calculated as 112 per 100,000 taking all the cases selected for study as poliomyelitis and ignoring the cases with a longer time before reporting. With the same selected cases the rate was 246 per 100,000 for the most heavily hit districts of Cairo. It is noted that these rates are probably underestimates and are even so about 4 times higher than similar figures obtained by HALL *et al.* [*ibid.*, 1959, v. 34, 865] for the southern United States. *A. J. Beale*

DE SOUSA, J. C. Contribution à l'étude de la poliomyélite dans les îles du Cap-Vert. [**Studies on Poliomyelitis in Portuguese West Africa (Cape Verde Islands)**] *Ann. Inst. Pasteur.* 1960, Aug., v. 99, No. 2, 202–9, 6 figs.

The English Summary appended to the paper is as follows:—

"Qualitative studies on poliomyelitis antibodies in 288 normal and 31 diseased children in San Tiago (Cape Verde Islands) demonstrate that the incidence of polioviruses is very high in the island, and that children come very early in contact with them.

"Antibodies to type II appear later than antibodies to types I and III.

"The results suggest that the outbreak of San Tiago was caused by type I poliovirus."

GELFAND, H. M., FOX, J. P., LEBLANC, Dorothy R. & ELVEBACK, Lila. **Studies on the Development of Natural Immunity to Poliomyelitis in Louisiana. V. Passive Transfer of Polioantibody from Mother to Fetus, and Natural Decline and Disappearance of Antibody in the Infant.** *J. Immunology.* 1960, July, v. 85, No. 1, 46–55, 3 figs. [17 refs.]

During their valuable studies of natural immunity to poliomyelitis in Louisiana [this *Bulletin*, 1958, v. 33, 931 *bis*; 1959, v. 34, 1231; 1960, v. 35, 478, 1216.] Fox and his colleagues collected sera from many pregnant women and umbilical cord samples from their infants. They were thus able to study the passive transfer of maternal antibodies and the decay of these antibodies in the infant. They found in general that there was a close correspondence in maternal antibody titre and cord blood titre. There was if anything a tendency for cord blood titres to be lower and this was most clear for type 3 poliovirus antibodies. Also some individuals appeared to pass antibodies across the placenta sometimes of only one type considerably less efficiently than normal. Antibodies declined exponentially with a half life of about 25 days. In this population where poliovirus infection is prevalent and antibodies to all 3 types of poliovirus very prevalent in mothers, 50% of children lack antibodies by 3 months to one or other type of poliovirus. The authors accordingly recommend that poliovaccination be started at this age unless an adequate prenatal poliovaccination programme is operative.

A. J. Beale

LÉPINE, P., ROGER, F. & ROGER, A. Valeur pratique de la "technique cinétique" de séro-neutralisation pour le diagnostic sérologique de la poliomyélite. [**Practical Value of the Kinetic Seroneutralization Technique**] *Ann. Inst. Pasteur.* 1960, July, v. 99, No. 1, 1–12.

The authors have previously described their technique of performing poliovirus serum neutralization tests [this *Bulletin*, 1960, v. 35, 93]. In this paper they advocate this method as simple and economical for use in a diagnostic laboratory. They believe that a serum neutralization test is superior to complement fixation and virus isolation, either on the grounds of ease and reproducibility of performance or economy. They show many illustrative examples. They found that 78% of all cases diagnosed virologically could be satisfactorily diagnosed by serology alone. *A. J. Beale*

DAGUET, G. L. Séroneutralisation des virus poliomyélitiques. [**Seroneutralization of Polioviruses**] *Ann. Inst. Pasteur.* 1960, July, v. 99, No. 1, 103–13.

The value of the serum neutralization technique for poliovirus described by LEPINE *et al.* [this *Bulletin*, 1960, v. 35, 93] is illustrated in epidemiological studies in Paris involving the titration of over 3,000 serum samples against all 3 types of poliovirus. In a study of 2,060 sera from infants and adolescents it was found that 11% were triple negative (average age 6 years) and 32% triple positive (average age 18 years). The value of the method for following the response to poliovaccination and for the specific diagnosis of poliomyelitis is illustrated.

A. J. Beale

BENEDETTO, A., CORSO, P., MANCINI, L. & SCAFI, M. L'intradermoreazione con antigen poliomielitici in rapporto al tasso di anticorpi neutralizzanti. [**The Intradermal Reaction with Poliomyelitis Antigen in Relation to the Titre of Neutralizing Antibodies**] *Arch. Ital. Sci. Med. Trop. e Parassit.* 1960, Aug., v. 41, No. 8, 413–24.

The English summary appended to the paper is as follows:—

"The authors have studied intradermoreaction by poliomyelitic antigen as regards the serum ratio of neutralising antibodies in 20 poliomyelitic patients, in 16 individuals with poliomyelitic sequelae and in 6 healthy individuals who had been vaccinated with Cox's trivalent oral vaccine.

"They conclude that there is no relation between the positivity of the intradermoreaction and the ratio of the neutralising serum antibodies."

LANGMUIR, A. D. **Progress in Conquest of Paralytic Poliomyelitis.** *J. Amer. Med. Ass.* 1959, Sept. 19, v. 171, No. 3, 271–3, 3 figs.

This is a paper given by the Chief of the Epidemiology Branch of the Communicable Disease Centre to the Section on General Practice of the American Medical Association on June 9, 1959. He reviews the recent epidemiology of poliomyelitis since the introduction of poliovaccine and concludes that the vaccine is 75% effective. Epidemics are now concentrated among pre-school children in the poorer (often Negro) sections of large towns. He enjoins the help of local medical societies as well as health departments and National Foundation Chapters in promoting the widespread use of killed poliovaccine. If this is achieved large-scale epidemics, like the one in Detroit in 1958, should become a thing of the past. The theme of this paper is that the means of eliminating paralytic poliomyelitis are now to hand. All that is required is vigorous leadership of vaccination programmes. *A. J. Beale*

IANNI, F. A. J., ALBRECHT, R. M., BOEK, W. E. & POLAN, Adele K. **Age, Social, and Demographic Factors in Acceptance of Polio Vaccination.** *Pub. Health Rep.* Wash. 1960, June, v. 75, No. 6, 545–56. [11 refs.]

One of the most important problems remaining in the prevention of poliomyelitis is persuading people to receive poliovaccination. A study was made of the poliovaccination rate in a random sample of households in 2 counties in New York State, Rensselaer and Westchester. It was found that the poliovaccination rate was higher in females at all ages than in males and that there was a marked fall-off in the vaccination rate over the age of 15 years and under the age of 6 months. The best vaccinated age-group was the 5–9 years but even in the best vaccinated county, Westchester, only 66·5% for males and 69·9% for females had received a full course of 3 doses of vaccine. An analysis was also made by social class and it was found that in general the higher the social class the more likely the people in the household were to be vaccinated. However, there was some evidence that the people in education class II or social class II tended to accept vaccination more readily than those in the higher social or educational class. The acceptance rate for vaccine was higher in Westchester than in Rensselaer and Westchester enjoyed a much higher economic standard. The most frequent reasons given for failure to be vaccinated were that the individuals were too old. Individuals who were 20 to 29 as well as those who were over 40 frequently felt that they were too old to need vaccination and the authors believe that posters showing children suffering from the disease have created a more powerful image of the disease in the population than the propaganda directed at the young adults. The other prominent cause was due to apathy or neglect. Individuals were also asked why they thought that most teenagers had not been vaccinated and most ascribed the blame to the laxity of the parents. *A. J. Beale*

GRIST, N. R. & DUNCAN, I. B. R. **Poliomyelitis-Like Illnesses after Poliovaccination.** *Health Bull.* (Issued by the Chief M.O., Dept. of Health, Scotland.) 1960, July, v. 18, No. 3, 37–8.

The authors illustrate the importance of supporting a clinical diagnosis of poliomyelitis by laboratory investigations by presenting the results of investigations on 14 patients notified to Medical Officers of Health in Scotland as cases of poliomyelitis in vaccinated persons during March to December 1959. It is already well known that cases of aseptic meningitis are rather rarely due to polioviruses but it is also becoming apparent that cases of paralytic poliomyelitis may sometimes be due to viruses other than polio. In all, 14 cases were notified. 8 of these were paralytic and one of them was fatal. Subsequent investigation showed that 2 of these patients had not in fact been vaccinated, one of these was excreting a Coxsackie B2 virus and the other a type 1 poliovirus. The patient who died was excreting Coxsackie A7 as were 2 of the remaining 5 paralytic cases. No virus was isolated from 2 of these cases and an as yet unidentified enterovirus was isolated from the remaining patient. 4 patients were classified as suffering from aseptic meningitis; 2 yielded a Coxsackie A7 virus and one of these was also excreting an adenovirus type 2. From the remaining 2 patients no virus was isolated. There were in addition, 2 other patients, one suffering from arm weakness after chicken pox and the other one suffering from a spasm in the foot and pneumonia, and neither of these patients yielded a virus. No serological studies on these patients are reported and the authors note the importance of obtaining an acute and convalescent specimen so that such studies can be undertaken although they are often less illuminating than virus isolation. They also call attention to the importance of obtaining material from the brain and spinal cord for virus isolation. Unfortunately, in their case, such unfixed brain tissue was not available and the only isolation was made from stools. It is interesting that 3 of the 6 viruses isolated from the 8 cases of "paralytic poliomyelitis" were Coxsackie A7 virus which was originally termed poliovirus type 4 by the Russian workers CHUMAKOV *et al.* (*Problems of Virology*, 1956, v. 1, 16). *A. J. Beale*

SLOME, R. & YUDELMAN, H. **Sensitivity Reaction to Poliomyelitis Vaccine.** *South African Med. J.* 1960, Aug. 6, v. 34, No. 32, 666.

Report of a case with tetany ascribed to the penicillin content of the vaccine.

CALARESU, I. & SALIS, M. Su due casi di glomerulonefrite acuta emorragica consecutivi a vaccinazione antipoliomielitica. [**Two Cases of Acute Haemorrhagic Glomerulonephritis after Vaccination against Poliomyelitis**] *Giorn. di Malattie Infettive e Parassit.* 1960, May–June, v. 12, Nos. 5/6, 296–9.

MELNICK, J. L. **Problems associated with the Use of Live Poliovirus Vaccine.** *Amer. J. Pub. Health.* 1960, July, v. 50, No. 7, 1013–31, 4 figs. [27 refs.]

In this paper Melnick has stressed the difficulties associated with the use of attenuated poliovirus vaccine. He first considers the methods available for the selection of attenuated strains and then presents results of a comparison of the monkey neurovirulence of the Lederle and the Sabin strains of attenuated poliovirus. The results show clearly that in equal dosage the Sabin strains are much less virulent than the Lederle strains. He presents a long discussion of the genetic stability of the attenuated strains of poliovirus, mainly dealing with isolates from persons fed the Sabin strains. He has tested these isolates for the d and the t characters and also for monkey neurovirulence both after intramuscular and intraspinal inoculation. As far as the d and the t characters were concerned, it was found that type 1 poliovirus was relatively stable. 19 out of a total of 37 isolates from persons fed the type 1 strain remained d− t− whereas only 3 out of 25 type 2 strains and 1 out of 23 type 3 strains retained the d− t− characters. Whereas strains that retained the d− t− characters required about 10^4 TCD50 in order to paralyse 50% of monkeys after intraspinal inoculation, 10 TCD were sufficient to paralyse monkeys when there had been a reversion to d+ t−. The d+ t+ strains were found to be even more virulent, producing paralysis not only by the intraspinal but also by the intracerebral route. When the intramuscular route of inoculation was used instead of inoculation directly into the central nervous system broadly similar results were obtained. The d− t− vaccine strains only caused localized lesions [KIRSCHTEIN *et al.*, this *Bulletin*, 1960, v. 35, 1144] have shown that the Cox and Koprowski type 1 strains cause paralysis in large doses intramuscularly]. The isolates that were d+ t− produced mild central nervous lesions with mild clinical disease whereas the d+ t+ strains produced more severe lesions and, in most of the animals, viraemia. A few strains that are t− but nonetheless virulent for monkeys are also described, which points out the limitations of the t marker as a guide to the virulence of strains. The author concludes that the strains are genetically unstable and must, therefore, represent a danger to the contacts of vaccinated persons. It has been suggested that this problem could be overcome in large measure by the mass immunization of the population but Dr. Melnick is doubtful whether such a programme would prove acceptable to the American people and fears, therefore, that contact infections with virus that has reverted to greater virulence may well occur. He also points out that the presence of wild enteroviruses can severely inhibit the effectiveness of attenuated polioviruses. Thus, in a study of 82 serologically susceptible children fed Sabin vaccine in Mexico City, only 37 were shown to have a detectably antibody rise to the appropriate type of vaccine virus. Of 28 children from whom no wild enterovirus was isolated, 22 excreted the poliovirus and showed an antibody rise, whereas 33 out of 47 children who were found to be excreting another enterovirus did not produce antibodies to the fed attenuated poliovirus. He therefore concludes that even under condition of mass feeding many persons will escape infection with the attenuated virus and may later become infected by contact with a virus excreted from a successfully vaccinated individual.

[SABIN and his colleagues [see below] advocated letting nature supplement the effect of the vaccine in his study in Toluca where he was attempting to solve the problem of immunizing a population with a highly prevalent wild enterovirus flora.] *A. J. Beale*

SABIN, A. B., RAMOS-ALVAREZ, M., ALVAREZ-AMEZQUITA, J., PELON, W., MICHAELS, R. H., SPIGLAND, I., KOCH, M. A., BARNES, Joan M. & RHIM, J. S. **Live, orally given Poliovirus Vaccine. Effects of Rapid Mass Immunization on Population under Conditions of Massive Enteric Infection with other Viruses.** *J. Amer. Med. Ass.* 1960, Aug. 6, v. 173, No. 14, 1521–6, 5 figs.

A serious difficulty has occurred in the application of attenuated poliovaccine programmes in areas with climatic and hygienic conditions favouring the spread of enteric viruses. This is because the wild enteric viruses interfere with the establishment of attenuated poliovirus infection, at least under the systems of administration usually employed (*e.g.*, vaccination of only a small fraction of the population at one time). This paper describes a successful method of overcoming this problem.

In Toluca, Mexico, 86% of the child population received a trivalent mixture of Sabin's attenuated poliovaccine ($10^{5\cdot2-5\cdot6}$ TCD50 of each virus type) in a mass campaign reaching 97% of them in 4 days. A survey before starting showed that enterovirus infection was very prevalent, 72% of the children of 1 year excreting an enterovirus and 14–15% of the children between 7 months and 2 years excreting polioviruses. Also 5% of the mothers excreted a poliovirus. As might be expected from these figures, antibodies to poliovirus are rapidly acquired in Toluca. Indeed, by 4 years over 90% of the children have antibodies to each of the 3 types of poliovirus. During this natural immunization process, on the average 14 cases of paralytic poliomyelitis occur each year. In 1950, 20 cases had already occurred when the vaccination programme began in August.

After the feeding of poliovaccine the isolation rate for non-polio interoviruses did not vary but for polioviruses it increased to between 40–70% depending on the age-group. 3 months later, however, the poliovirus infection rate had declined to 0·7%—a 16-fold lower rate than before the programme was initiated. The serological conversion rates in a small sample were type 1 68%, type 2 82% and type 3 43%. The rates of conversion for types 1 and 3 were much higher in those who had got type 2 antibodies, suggesting that the type 2 component of the vaccine was dominant. These figures compare unfavourably with the rates observed when feeding

the types separately in temperate zones where the conversion rates exceeded 90% for all 3 types. Very few children became serologically positive between 10 and 21 weeks after feeding. 44 children who remained negative were given another dose of trivalent vaccine and the cumulative conversion rate became for types 1 and 2 96% and for type 3 72%. Study of the control city of Queretaro showed that a substantial degree of extra poliovirus immunity had been acquired in Toluca as a result of the administration of Sabin's strains of poliovaccine.

[This is a very impressive study involving a vast amount of work. It deserves to be read in the original. Technical details of laboratory and field methods are sparse. As the authors say, this study is of importance to the majority of the human population living under conditions of high endemicity of polio and other viruses. The cost in paralysis of such naturally acquired immunity may be high, as illustrated in a recent paper from Egypt, see this *Bulletin*, 1960, v. 35, 1212.] *A. J. Beale*

PAGANO, J. S., PLOTKIN, S. A., JANOWSKY, C. C., RICHARDSON, Suzanne M. & KOPROWSKI, H. **Routine Immunization with Orally Administered Attenuated Poliovirus. A Study of 850 Children in an American City.** *J. Amer. Med. Ass.* 1960, Aug. 27, v. 173, No. 17, 1883–9, 1 fig. [20 refs.]

Despite the widespread use of killed poliovaccine, epidemics of poliomyelitis still occur in the United States. These epidemics for the most part are concentrated among non-vaccinated people in poorer sections of big towns and affect particularly children under 5 years. The authors decided to attempt to overcome this problem in Philadelphia with a trial of attenuated orally administered poliovaccine. 335 children aged 1½ months to 5 years were given all 3 types of vaccine. Each type of virus was given separately in a dose of approximately 5·7 TCD50. The strains used were CHAT type 1, P 712 type 2 (from Dr. Sabin) and W-Fox type 3.

850 children received type 1 vaccine and 805 type 3 as well. 52% of the children were aged 1½–6 months, an age-group that is vulnerable to poliomyelitis but responds poorly to Salk type vaccine. There was no evidence of any untoward effects of vaccination either on the vaccinated subjects or on the community. The children came from 830 households containing 991 children of a susceptible age-group but no case of poliomyelitis occurred among them. 22 virologically proven cases of poliomyelitis occurred in Philadelphia in 1959 and 11 of them were from the study districts but there was no evidence that these cases were due to the vaccine strains and there were none in the vaccinated children or their households. Indeed, the incidence of poliomyelitis was no greater than might have been expected.

The serological response to vaccine strains was good. Over 90% of the children between 1½ and 6 months responded to all 3 types of virus regardless of whether maternal antibodies were present or not. A similar sort of response occurred in children aged 6 months to 6 years who lacked antibodies, but was much less good in those with prior antibodies. The median titres to the 3 types in subjects who lacked antibodies before vaccination were between 1 in 32 and 1 in 128.

A. J. Beale

GELFAND, H. M., LEBLANC, Dorothy R., POTASH, L., CLEMMER, Dorothy I. & FOX, J. P. **The Spread of Living Attenuated Strains of Polioviruses in Two Communities in Southern Louisiana.** *Amer. J. Pub. Health.* 1960, June, v. 50, No. 6, Pt. 1, 767–78, 1 fig. [11 refs.]

This paper continues the illuminating series of studies on the transmission of polioviruses undertaken by Fox and his colleagues [this *Bulletin*, 1957, v. 32, 1031; 1958, v. 33, 931 *bis*; 1959, v. 34, 112, 1231, 1300]. One of the remaining doubts about attenuated poliovaccine has been whether the virus may spread to contacts and revert to virulence and thus initiate outbreaks of the disease it is desired to eradicate. Both reversion to greater virulence and spread to contacts have been observed. This study was aimed at determing the amount of spread that would occur in a lower economic American population during the summer months. Accordingly study areas were set up in Morgan City (133 households) and Franklin (75 households) in Southern Louisiana. In Morgan City 12 families (55 children) were fed type 3 Sabin vaccine in a dose of $10^{7·3}$ TCD50 and 13 matched families (69 children) a placebo. In Franklin 13 families (56 children) were fed vaccine and 13 (51 children) were fed a placebo. A total of 71 presumed susceptible children were fed vaccine and 64 became infected with the vaccine strain. Virus spread to 15 out of the 26 placebo-fed households and 26 out of 67 susceptible children in these families became infected. Not only was spread to contacts less frequent than had been expected but also the duration of excretion was less in contact infections than in those fed virus. Moreover, unlike wild poliovirus infections in households, many susceptibles in a family escaped infection when 1 member became infected by contact. Preliminary studies would indicate that the rarity of contact infections could well have been due to the prevalence of interfering enteroviruses. Despite the very high dose of vaccine administered interference was a probable cause of some of the 10% failures to achieve infection. More failures would be likely with a lower dose of vaccine. The authors conclude from this study that contact spread is not very likely to occur in a community and that therefore fears about reversion to virulence need not be too serious and that hopes of a spreading involuntary community vaccination from a focus of vaccine-fed individuals are likely to be frustrated. *A. J. Beale*

DÖMÖK, I., MOLNÁR, Elizabeth & RUDNAI, O. **An Epidemic of Bornholm Disease in Hungary in 1958.** *Acta Microbiologica.*, Budapest. 1960, v. 7, No. 2, 151–68, 2 figs. [31 refs.]

This paper describes an immense epidemic of Bornholm disease that occurred in Hungary in 1958. This involved more than 40,000 people. The epidemic started

in the west of the country and spread eastwards and extended from June to September. During the epidemic there were 2 outbreaks of myocarditis and meningo-encephalitis among newborns in maternity wards. The epidemic and the outbreaks among newborns were shown clearly to be due to Coxsackie B3 virus which was isolated from 65% of the patients with Bornholm disease and from 62% of the newborns with myocarditis. 86% of the patients with Bornholm disease had antibodies to Coxsackie B3 virus upon recovery. By contrast only 19% of the patients suffering from other diseases had Coxsackie B3 antibodies and only 13% yielded a Coxsackie B3 virus. Most of the strains of Coxsackie B3 could be isolated both in monkey kidney cells and in suckling mice but a significant number of strains would only grow in suckling mice on first isolation. 1 out of 9 of the affected newborns died in the first outbreak and 3 out of 22 in the second outbreak. In addition to Coxsackie B3 virus a few other enteroviruses were also isolated as follows. Thus, from 523 stool specimens, 241 enteroviruses were isolated, 219 Coxsackie B3, 1 each of Coxsackie A5, A6, B1 and B4, 2 Coxsackie B2, 1 each of ECHO 1, 7, 8 and 14, 3 ECHO 9, 2 type 1 polio and 1 each of types 2 and 3. The authors note also that during 1958 there was a remarkably low incidence of poliomyelitis. This, they believe, may well have been an example of the antagonism between Coxsackie B and polioviruses that has been postulated to exist by Dalldorf (*Ann. Rev. Microbiol.*, 1955, v. 9, 277). They believe that this antagonism is a much more likely explanation for the low level of poliomyelitis in 1958 than the extensive programme of Salk vaccination which was instituted in 1957 and followed up in 1958 with booster doses. This is mainly because in 1959 there was a severe epidemic of poliomyelitis in Hungary. *A. J. Beale*

Lippi, M., Frugoni, G. & Corso, P. Contributo sieroimmunologico alla conoscenza delle principali virosi. Ricerca nei soggetti sani degli anticorpi devianti il complemento verso il virus ECHO 9. [**Study of Complement Fixing Antibodies to ECHO 9 Virus in Healthy Subjects**] *Arch. Ital. Sci. Med. Trop. e Parassit.* 1960, July, v. 41, No. 7, 337–80, 2 graphs. [118 refs.]

The English summary appended to the paper is as follows:—

"The authors have studied the antibodies fixing the complement on the antigens of the ECHO 9 virus (Vispo strain) in three groups of individuals divided as follows:

'A) a sample of the healthy population of Rome consisting in 459 individuals;

"B) 78 adult subjects of both sexes, belonging to an agricultural community in the area of Rome;

"C) 62 children from a hospital for bone TBC.

"In the first group there was a percentage of antibodies equal to 1:4 or higher, i.e. 21.6% of the cases, in the second group 19.2%, in the third 25.8%.

"In the introductory part the authors have reviewed the main characteristic and the epidemiologic data concerning the ECHO viruses."

Buşilă, V. T., Stambuliu, D. W., Popian, R., Cucuruz, L., Alexandrescu, R., Iavorovschi, V. & Negoescu, E. Asupra unor epidemii familiale de hepatită epidemică de contact. [**Some Familial Epidemics of Contact Epidemic Hepatitis**] *Microbiol., Parazitol., Epidemiol.* Bucharest. 1960, Mar.–Apr., v. 5, No. 2, 143–8. [18 refs.] English summary (7 lines).

Between 1954 and 1957 the authors carried out an epidemiological investigation of infective hepatitis in a town in Rumania, in which over 60% of the notified cases were studied [the total number is not stated]. Transmission by contact was established in 32% of cases and was the probable method of transmission in 24·1%. Two cases occurred in each of 118 families studied, 3 in 12, and 4, 5 and 6 cases each in 3 families.

D. J. Bauer

Mitroiu, Otilia, Predoviciu, Felicia & Popa, M. Valoarea testului aldolazei serice în diagnosticul hepatitelor epidemice. [**Value of the Serum Aldolase Test in the Diagnosis of Epidemic Hepatitis**] *Microbiol., Parazitol., Epidemiol.* Bucharest. 1960, Mar.–Apr., v. 5, No. 2, 149–54. [17 refs.] English summary (7 lines).

The authors have investigated the serum aldolase activity in 189 patients suffering from suspected infective hepatitis and 361 admitted with a diagnosis of the disease, and in 805 normal persons and 108 patients suffering from other diseases. Among the patients with infective hepatitis in whom the diagnosis was confirmed (435) serum aldolase levels of 20–40 units were found in 108 and of 40 units or higher in 327. In the control patients the values did not exceed 40 units, and values of 20–40 units were found in only 28 normal persons, and in 5 of 33 patients with chronic illnesses and 38 of 42 with various types of liver involvement. From the results obtained it is concluded that values of 40 units or higher confirm the diagnosis of infective hepatitis, whereas values below 20 units exclude it and values of 20–40 are inconclusive. *D. J. Bauer*

Kranendonk, O., Borst, J. & Ruys, A. C. Het gevaar van serumhepatitis bij intracutane injecties: een experimentele oriëntering. [**The Hazard of Inoculation Hepatitis due to Intracutaneous Injections: an Experimental Orientation**] *Nederl. Tijdschr. v. Geneesk.* 1960, Aug. 13, v. 104, No. 33, 1576–82. [28 refs.]

The English summary appended to the paper is as follows:—

"Experiments on a guineapig with bacteriophage as virus indicator have shown that syringes used for intracutaneous injections are regularly contaminated.

"The infection may be transmitted even if platinum needles are used which are flamed after each injection. This occurs regularly with the 'multiple dose per syringe technique' and even, though less frequently, with Fleming's method, in which the syringe is filled with only

one dose at a time and the needle is flamed between injections with the plunger still pressed down.

"It follows that even with intracutaneous injections the only way to eliminate the risk of post-inoculation hepatitis is the use of a separate sterilized syringe and needle."

FAVORITE, F. G. **Some Evidence of Local Origin of EEE Virus in Florida.** *Mosquito News.* 1960, June, v. 20, No. 2, 87–92. [14 refs.]

In Florida in 1956 there were 107, in 1957, 386, and in 1958, 94 equine cases of encephalitis but numerous attempts at isolation of virus from mosquitoes had failed. 10 equine cases occurred in the study area in the year of this study. Mosquitoes were caught between March and July by means of light-traps: 8 genera and 24 species were caught, including 215 *Culiseta melanura* and 154 *Mansonia perturbans.* Inoculation of these intracerebrally into adult mice, however, resulted in no virus isolations. 320 wild birds of 44 species were taken by nets or shooting in spring and early summer 1958. Sera from 96 had neutralizing antibody against eastern equine encephalitis virus: 4 had also antibody to western equine virus. 17 of 23 of these sera had haemagglutinin-inhibiting antibody to eastern virus, while 14 of 42 sera without neutralizing antibody had haemagglutinin-inhibiting antibody.

Eastern equine virus was isolated from the blood of 6 birds, 3 of them collected on the same day at the same place. The species were rusty blackbird (?), meadowlark, tufted titmouse, Carolina wren, towhee and bluebird.

C. E. Gordon Smith

CHOU, Hsüeh-Chang. **Epidemic Type B Encephalitis: Its Clinical Manifestation and Treatment with Traditional Chinese Medicine.** *Chinese Med. J.* Peking. 1960, v. 80, No. 6, 548–53.

251 cases of Japanese encephalitis were observed in Chiahsing in 1954–58. 225 of them were from rural areas. 79% of the patients were under 10 years of age and there were 158 males to 93 females. Most occurred between mid-July and mid-August. The mortality ranged from 29% of 35 cases in 1955 to 9% of 122 cases in 1958—it was highest (about 20%) in children aged 3–6 years.

The illness had a sudden onset of high fever, headache and vomiting followed by cerebral symptoms: 80% had convulsions and 69% coma. Retention of urine was seen in 11% and incontinence in 45%. [The text and table disagree about which percentage applies to which.] Neck rigidity and Kernig's sign were present in 94% and Babinski's sign in 81%. Hemiplegia occurred in 17 and paraplegia in 9 patients. 79% had leucocyte counts over 10,000 per cmm. Lumbar puncture was performed in 242 patients: 82% had cell counts between 21 and 500 per cmm. In 13 cases diagnosed by complement-fixation or virus isolation, cell counts were below 10 per cmm. The sugar content was normal in 98% of cerebrospinal fluids. The chloride was 650–800 mgm.% in 88%.

By using a complement-fixation test [no technical details] Japanese encephalitis antibody was found in 13 of 93 patients where a single serum was examined [the authors do not state whether diagnostic rises in titre were demonstrated]. 2 strains of Japanese encephalitis virus were isolated from 9 cerebrospinal fluids obtained by cisternal puncture of fatal cases. [All this cannot be accepted as proof that the majority of the patients described were in fact suffering from Japanese encephalitis.]

28 of these patients had schistosomiasis. Neurological sequelae occurred in 53 of the 211 patients who survived.

173 patients were treated with traditional Chinese medicine [apparently mainly herbal] with a mortality of 7%, and 78 by western medicine with a mortality of 18% [but evidence is lacking that this was a properly designed treatment comparison].

C. E. Gordon Smith

BRODY, J. A. & BROWNING, G. **An Epidemic of St. Louis Encephalitis in Cameron County, Texas, in 1957.** *Amer. J. Trop. Med. & Hyg.* 1960, July, v. 9, No. 4, 436–43, 1 fig. [19 refs.]

Cameron County is flat and semi-tropical with extensive agriculture and irrigation. Between January and mid-June 1957 over 20 inches of rain fell but from then until the end of August was dry. This permitted standing water to become concentrated in organic and inorganic materials, a situation which apparently favours breeding of *Culex pipiens quinquefasciatus* [*fatigans*], the common vector of St. Louis virus east of the Rockies. *Psorophora confinnis, Aëdes vexans, Aëdes sollicitans* and *Anopheles quadrimaculatus* were also plentiful but very few *C. tarsalis* were found. St. Louis virus was isolated from 8 pools of about 50 *C. quinquefasciatus.* There was an unusually large wild-bird population in 1957.

114 encephalitis cases were reported in a population of 74,000 inhabitants. In 25 patients a significant rise in St. Louis complement-fixing antibody was demonstrated. 3 patients died, aged 60, 84 and 86. 2 cases occurred in June, 72 of them in the first half of August, and the last on August 23. The overall clinical attack rate was 155 per 100,000 but among airmen on a nearby base it was 280 per 100,000. There was an excess of male cases (65) over female (49) probably because of migrant labourers and day labourers. The age of patients ranged from 14 months to 86 years, half of them being 20–40 years. The incidence was 24% in patients over 60 whereas in 1950 this age-group accounted for only 7% of the population.

27 of 150 airmen and 111 of 367 civilians who had remained healthy throughout the epidemic were subsequently found to have complement-fixing antibody. These gave inapparent infection rates of 18% and 30% respectively and ratios of apparent/inapparent infections of 1 : 64 and 1 : 209. The age distribution of inapparent infections was the same in all groups suggesting that the higher incidence in over-60s was not due to increased exposure but to increased morbidity.

C. E. Gordon Smith

WHITMAN, L. & AITKEN, T. H. G. **Potentiality of *Ornithodoros moubata* Murray (Acarina, Argasidae) as a Reservoir-Vector of West Nile Virus.** *Ann. Trop. Med. & Parasit.* 1960, June, v. 54, No. 2, 192–204.

The Egypt 101 strain of West Nile virus after 1 mouse and 4 chick embryo passages was used. Stock ticks were maintained at 26°C., infected ticks at 30°C. Infant mice have a viraemia reaching 10^{-6} or more, 3–4 days after infection: first nymphs of *O. moubata* were allowed to feed on the 3rd day. The mean virus titres following such a feed were 4·8 log (3·6–6·1 log) immediately, 5·5 log (4·6–6·3 log) after 3 days incubation, >6·6 log (6·0–7·2 log) after 7 days, 5·7 log (5·3–6·7 log) after 14 days, 5·0 log (4·3–5·8 log) after 21 days, 4·3 log (2·7–5·3 log) after 35 days, and 2·7 log (<2·0–3·1 log) after 49 days. This gradual fall in titre was followed by a rise of 2·0 log or more 63–77 days after feeding. Second nymphs showed increases of 1·4 log 7 days after blood meals taken 5–9 weeks after infection. The percentage of ticks infected fluctuated without significant fall from 5 to 63 days after infection.

8 of 27 feedings on one-day-old chicks by groups of 4–11 infected nymphs 18–32 days after infection, transmitted infection. No subsequent feedings up to 98 days after infection resulted in transmission. Transmission attempts to suckling mice failed although two-thirds of the nymphs were shown to contain virus. In order to find out whether infection might be due not to tick-bite but to penetration of the skin by tick excreta, coxal fluid from infected adult females was tested for virus. Virus was present in the coxal fluid of 6 of 8 ticks. Transovarial transmission was not demonstrated. When stages from second nymphs to adults were fed on chicks in batches of 20 or more, transmission was achieved from 11 to 84 days after infection. The authors feel that the evidence suggests that infection is due rather to surface contamination with tick excreta than to infective bite.

Virus from a tick infected 188 days earlier was found to infect *Aëdes aegypti* by inoculation. *O. moubata* infected with Semliki Forest, Bunyamwera and Oriboca viruses remained infected for short periods only. West Nile virus was detected in adult *Dermacentor variabilis* which had been infected as larvae but no transmission was demonstrated. *C. E. Gordon Smith*

HANZAL, F. **Hyperimmune Gamma-Globulin in the Prophylaxis and Treatment of Tick-Borne Encephalitis.** *Rev. Czechoslovak Med.* Prague. 1959, v. 5, No. 3, 186–91. [14 refs.]

Hyperimmune gamma-globulin was prepared from the serum of persons who had had tick-borne encephalitis a year or more previously. The neutralizing indices of 6 batches of 10% gamma-globulin were 2,300–252,000.

8 patients with meningitic or encephalitic tick-borne encephalitis were given 1 or more doses of 3–9 ml. gamma-globulin without detectable effect on the course of their illness. 4 patients were given 6 ml. of gamma-globulin in 1 or 2 doses on the first or second day of illness but all were subsequently admitted to hospital with meningitis or encephalitis. 4 patients were given gamma-globulin prophylactically within 2 days of tick-bite—none developed clinical tick-borne encephalitis and complement-fixation tests on paired sera did not reveal a significant increase in antibody. It is therefore uncertain whether these patients had been infected. 3 patients given gamma-globulin soon after the onset of symptoms recovered without neurological involvement—such abortive cases are, however, not uncommon.

The only conclusion that can be drawn is that there is little or no evidence of beneficial effect when gamma-globulin is administered after the onset of symptoms.

C. E. Gordon Smith

LE ROUX, J. M. W. **The Histopathology of Wesselsbron Disease in Sheep.** *Onderstepoort J. Vet. Res.* 1959, Dec., v. 28, No. 2, 237–43, 5 figs.

Liver, spleen, myocardium, kidney, intestine, gall-bladder, and lung tissues were obtained from sheep and lambs in an outbreak of Wesselsbron disease in the Middelburg District in the autumn of 1956–57. The disease occurred in widely differing degrees of severity. Post mortem examination revealed jaundice, scattered haemorrhages in the subcutis, intermuscular connective tissue, heart and intestines. The serous cavities contained blood-stained or yellow fluid. In acute and subacute infections the liver was firm and golden yellow, and the gall-bladder enlarged and black.

Histologically the liver showed congestion and diffuse fatty infiltration. Cells were swollen and nuclear degeneration marked: eosinophil intranuclear inclusions were seen in 3 cases. Affected cells were diffusely scattered through the liver. There was diffuse bile pigmentation of liver and Kupffer cells. A deep blue pigment was also seen in Giemsa-stained sections: similar pigment has been previously (1928) described in enzootic icterus. The liver showed mononuclear infiltration around vessels and increased reticulo-endothelial activity.

There were congestion and fatty infiltration in the convoluted tubules of the kidney, haemorrhages in the myocardium, and hyperaemia, emphysema and mononuclear infiltration in the lungs. The spleen showed congestion, haemorrhages, and diminished cells in the malphighian bodies. The gall-bladder showed oedema, and haemorrhage which was also seen in the intestine.

The pathology and histopathology were, however, varied and difficulty would be found in diagnosing single cases of infection. Experimental infection of lambs produced similar but milder pathological changes. Only moderate fatty degeneration of the liver was found in experimentally infected mice.

Pregnant ewes vaccinated against Wesselsbron disease gave still-born lambs [incidence is not stated and type of vaccine is not described]. 7 of these foetuses were examined and found to give extensive meningo-encephalitis [the aetiology of this is, however, not clear].

C. E. Gordon Smith

RALSTON, L. S. & POWERS, W. T. **Orchitis as a Complication of Infectious Mononucleosis.** *J. Amer. Med. Ass.* 1960, July 23, v. 173, No. 12, 1348–9.

"A 29-year-old man, whose case is described, had infectious mononucleosis. His clinical course was complicated by both hepatitis and orchitis, the latter to our knowledge not having been reported previously."

OTHER COMMUNICABLE DISEASES

WARWICK, W. J. & GOOD, R. A. **Cat-Scratch Disease in Minnesota. I. Evidence for its Epidemic Occurrence.** *Amer. J. Dis. Children.* 1960, Aug., v. 100, No. 2, 228–35. [23 refs.] **II. The Family Epidemics.** *Ibid.*, 236–40. [12 refs.] **III. Evaluation of the Intradermal Skin Test to Cat-Scratch Disease Antigen.** *Ibid.*, 241–7. [21 refs.]

This paper, which is in 3 sections with separate lists of references, contains much interesting information and description of experience of cat-scratch disease which though unknown in the medical literature before 1950 is now being recognized in all parts of the world.

The first section contains a report on the study of 12 cases and 6 cases of the disease which were diagnosed in the Minneapolis-St. Paul area in the autumn and winter of 1955 and 1956. Before this only 1 case had been reported but reasons are given for assuming that actually cat-scratch disease is not a new disease in the area. The methods of study, epidemiological features (including estimates of cat population), diagnosis, clinical manifestations and seasonal incidence are described in some detail. There is evidence that in North America the incidence of cat-scratch disease is greatest between September and February, particularly in November and December.

The second section of the paper contains an account of the study of the family epidemic groups in particular relation to the cat.

The third section is on the preparation of cat-scratch disease antigens, the technique of the skin test and evaluation of results obtained with this test. Tests were performed on a considerable number of persons and it was found that in the general population 5·8% gave a positive result whereas in members of families exposed to the disease 26·4% were positive. Increased frequency of positives was also found in veterinary and medical personnel. *M. E. Delafield*

Bacteriology and Immunity

The order in this section is:—**General; Bacteriostatic and Bactericidal Substances; Bacteria; Rickettsiae; Bacteriophages; Viruses; Immunity.**

Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the TROPICAL DISEASES BULLETIN. *Their titles and page references are cited below in the appropriate sub-divisions of this section.*

GENERAL

MARSHALL, J. H. **The Production of Anaerobic Conditions with Chromous Salts.** *J. General Microbiol.* 1960, June, v. 22, No. 3, 645–8.

The rate and continuity of the reaction of sulphuric acid with chromium varies much with the quality of the metal and the absorption of O_2 by the chromous ion in acid solution will vary correspondingly. As a means of obtaining anaerobic conditions in a closed jar a more reliable absorption of O_2 is obtained by using granulated zinc and a solution of a chromic salt in H_2SO_4 instead of a chromium powder and sulphuric acid. A good indicator tube which can be used repeatedly is described as follows:

Methylene blue, 0·04% (w/v) in 0·2M-phosphate (*p*H 7)	1·0 ml.
Ascorbic Acid, 0·5% (w/v)	1·0 ml.
Agar, 0·6% (w/v)	8·0 ml.

J. W. McLeod

NEIDHARDT, F. C. & MAGASANIK, B. **Studies on the Role of Ribonucleic Acid in the Growth of Bacteria.** *Biochim. et Biophys. Acta.* 1960, July 29, v. 42, No. 1, 99–116, 4 figs. [30 refs.]

SMITH, D. D. & MILES, A. A. **The Role of Histamine in Early Bacterial Inflammation of the Rat Peritoneal Cavity.** *Brit. J. Exper. Path.* 1960, June, v. 41, No. 3, 305–12. [11 refs.]

The rat peritoneum is rich in histamine-liberating mast cells and is an excellent experimental system for investigating the action of histamine in infective inflammation. Rats were injected intraperitoneally with 15 ml. of isotonic salt solution containing minimal infective doses of *Pseudomonas pyocyanea, Corynebacterium ovis* and *Staphylococcus aureus.* Control rats were given the same suspensions killed by heat. The rats were killed at intervals and the peritoneal exudate removed. The peritoneum was washed out with 10 ml. of isotonic salt solution and the washings and exudate combined in order to measure the protein and free histamine.

Both test and control rats showed a slight rise in leucocytes in the peritoneal fluid after two to four hours —due largely to the suspending fluid. The protein content of the peritoneal washings was estimated spectrophotometrically and was found to be higher in the test than in the control series at all times. The free histamine was found not to exceed 2 μgm. in either case.

That a given level of free histamine is the result of

enhanced production and liberation of histamine in the presence of histaminase was tested. Compound 48/80 (a low polymer of substituted phenylethylamine and a potent histamine liberator) was incorporated in the washing fluid and allowed to remain for 20 minutes after killing. Histamine assay showed that this treatment increased the free histamine to 20 μgm. in both test and control rats. Thus the amount of unreleased histamine was the same in each case. Direct assay showed the absence of histaminase activity.

The antihistaminic triprolidine did not alter the protein concentration of the exudate of rats injected intraperitoneally with *C. ovis*. No difference was histologically detected in infected or control mast cells.

Less than 1 μgm. of 5 hydroxytryptamine was found in the infected or control washings.

The results of injection of staphylococcal α-toxin were similar to those with living cultures.

The conclusion is that histamine plays no essential part in early inflammation. *Stewart Fletcher*

RUYS, A. Charlotte, with the technical assistance of N. E. EDEL. **On the Nature of P.P.L.O. I. Bacteriological Observations.** *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1960, v. 26, No. 1, 1–8, 7 figs.

"In a number of strains of the three species of P.P.L.O. of human origin coccoid elements have been observed, which are Gram positive or Gram variable and of very small size (<0·5 μ). They are able to grow in pure culture on the surface of nutrient agar in very small colonies. Although they have bacterial characteristics, they could not be identified as known bacteria. Agglutination tests are in favour of a serological relationship between the coccoid elements and P.P.L.O. The suggestion that these elements might be an outside contamination is made unlikely by several observations. The supposition that P.P.L.O.s are L forms of these coccoid elements should be considered further."

BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

The order in this section is:—**General; Antibiotics; Colicines; Other Therapeutic Substances; Disinfection.**

FAIRBROTHER, R. W. & TAYLOR, G. **Observations on Penicillin "B".** *Lancet.* 1960, Aug. 20, 400–402.

"B" is an abbreviation of Broxil (the potassium salt of 6-(α-phenoxypropionamido)-penicillanic acid). These authors describe the evidence that this form of penicillin produces higher blood levels than penicillin V as "conflicting" (although in fact it is not so if allowance is made for the different methods of assay used in the 2 American studies which they quote) and therefore investigated the question themselves. They gave 250 mgm. of penicillin B and V to normal subjects, and obtained single specimens of blood at intervals varying from 35 to 80 minutes later, in which the antibiotic was assayed by a serial dilution method with the use of a staphylococcus equally sensitive to penicillins G, V and B. The concentrations found in μgm./ml. were: total range, V 0·48–4·32, B 1·08–6·72: overall means, V 1·98, B 3·06.

They then examined activity against numerous strains of staphylococci by a tube dilution test with a large inoculum in view of the finding of GARROD [this *Bulletin*, 1960, v. 35, 686] that B, owing to its slower inactivation by penicillinase, is inhibitory in lower concentrations than G in such a test unless the strain forms either very much penicillinase or very little. They confirmed this finding, but showed that the difference is greater (8–64-fold) when the inoculum is smaller (dilution 1/251) as compared with a 2–8-fold difference when the dilution is 1/26. They then argue that in view of the large amount of penicillinase likely to be present in an established staphylococcal lesion due to a resistant strain, the suggestion that penicillin B might be used in such infections "cannot be supported". [Among many authors who do not accept the view that penicillin is useless in such infections are ABBOUD and WAISBREN [*ibid.*, 469] who analysed 100 cases of staphylococcal septicaemia, and found that penicillin often succeeded when the staphylococcus was only moderately resistant, although never when it was highly so. Treatment here was with penicillin G. According to the findings both of the writer of this abstract and of the authors of this paper, penicillin B should be more effective.] *L. P. Garrod*

MCCARTHY, C. G. & FINLAND, M., with the technical assistance of Clare WILCOX & Joan H. YARROWS. **Absorption and Excretion of Four Penicillins: Penicillin G, Penicillin V, Phenethicillin and Phenylmercaptomethyl Penicillin.** *New England J. of Med.* 1960, Aug. 18, v. 263, No. 7, 315–26, 8 figs. [19 refs.]

Single 500 mgm. doses of penicillin in 6 different forms were given to normal young men before or after breakfast. The blood content was assayed in samples obtained ½, 1, 2 and 5 hours after the dose by 4 different methods —a tube dilution method with a staphylococcus, a haemolytic streptococcus and a pneumococcus, and the *Sarcina lutea* cylinder plate method. The content of the urine passed in the first 5 hours was also determined. The results, necessarily somewhat complex owing to the variety of methods used, are presented in 8 tables and 19 graphs.

Two of the preparations used were different forms (tablet and capsule) of phenethicillin (potassium alpha-phenoxyethyl penicillin: Broxil in Britain), and the principal object of the investigation appears to have been to examine the claims made for this product. It was confirmed that this gives higher w/v blood levels than penicillin V and that a somewhat larger proportion of the dose is excreted in the urine, but, owing to the lesser activity of phenethicillin against streptococci and pneumococci, this advantage is neutralized when the results are expressed in terms of activity of the serum against these organisms. The authors therefore suggest that "If various products are to be called penicillins, their activity should be indicated in terms of a standard unit such as that of penicillin G . . .". Of the other forms of penicillin tested, penicillin G given by injection (all others were given orally) produced higher levels, better sustained through the 5-hour period, than all the rest; a "long-acting" oral tablet of penicillin G gave lower initial levels but better sustained than those produced by other preparations up to and after the 5th hour; and phenylmercaptomethyl penicillin gave low w/v levels and a low percentage urinary excretion because of poor absorption, but a relatively higher degree of serum activity because of its own intrinsically greater activity. The effect of administration after a meal instead of fasting was to slow absorption, the peak serum level being reached later, and somewhat to reduce total absorption. *L. P. Garrod*

BOWMAN, Frances W. & HOLDOWSKY, S. **Production and Control of a Stable Penicillinase.** *Antibiotics & Chemotherapy.* New York. 1960, Aug., v. 10, No. 8, 508–14. [10 refs.]

GERONIMUS, L. H. **Inoculum Size and the Apparent Sensitivity of Staphylococci to Penicillins.** *New England J. of Med.* 1960, Aug. 18, v. 263, No. 7, 349–51. [74 refs.]

Broth containing different amounts of penicillin G and of alpha-phenoxyethyl penicillin (phenethicillin in the U.S.A.: Broxil in Europe) was inoculated with different numbers of a low penicillinase-producting staphylococcus. When the inoculum was about 10^3 cocci low concentrations of both penicillins inhibited growth: when it was 10^5 of 10^6 phenethicillin was much more inhibitory than penicillin G: when it was 10^8 the respective inhibitory concentrations of these 2 penicillins were 4,000 and $>4{,}000$ μgm./ml. "Since the number of viable staphylococcal units in a lesion can approach 10^{10} per gram, it seems rash to predict clinical effectiveness of either penicillin against a strain such as the one under consideration." It is also pointed out that conventional tests of such an organism employing a small inoculum can be most misleading. *L. P. Garrod*

GROUNDS, M. D. **Immediate Reactions to Procaine Penicillin Injection, with a Report of Three Cases.** *Med. J. Australia.* 1960, July 2, v. 2, No. 1, 15–16.

3 patients given a supposedly intramuscular injection of 600,000 units of procaine penicillin had immediate reactions described as "an alarming sensation of light-headedness and unreality", "a numb feeling all over", blurred vision, hot flush, weakness and (in 2 patients) deafness to deep notes, so that voices sounded like a "small cheap wireless" or "rattling". All were relieved by intravenous thiopentone, and the author believes that the antibiotic was in fact injected into a vessel (one injection was given with a cartridge syringe which did not enable the operator to detect whether he had perforated a vessel), and that the symptoms were due to procaine poisoning. *L. P. Garrod*

HANCOCK, R. **The Bactericidal Action of Streptomycin on *Staphylococcus aureus* and some Accompanying Biochemical Changes.** *J. General Microbiol.* 1960, Aug., v. 23, No. 1, 179–96, 10 figs. [32 refs.]

In this study it was first confirmed that streptomycin is bactericidal only when organisms are able to grow: the absence of nutrients or the presence of chloramphenicol prevents the effect. Anaerobiosis also greatly reduces it. Further studies concerned the metabolism of *Staphylococcus aureus* in the presence of bactericidal (10 μgm./ml. or more) concentrations of streptomycin. By adding amino acids labelled with ^{14}C it was shown that there was a reduced uptake of glutamic acid and alanine, and the same type of experiment showed a reduced incorporation of orthophosphate containing ^{32}P. The rate of synthesis of nucleic acid was diminished. Estimations of the respiratory quotient showed a reduced oxidation of glucose, glycerol, lactate and formate. The introduction contains the statement: "No published studies describing inhibitory effects of streptomycin on metabolic reactions have established that inhibition of the affected reactions is the primary cause of loss of viability of the organisms". It does not appear to be claimed that the work described here invalidates this statement. *L. P. Garrod*

HASHIMOTO, K. **Streptomycin Resistance in *Escherichia coli* analysed by Transduction.** *Genetics.* 1960, Jan., v. 45, No. 1, 49–62. [Numerous refs.]

SGARZI, B., LUGLI, A. M. & GIOLITTI, G. **An Antibiotic Complex derived from a *Streptomyces* and Active against Gram-Positive Bacteria.** [Correspondence.] *Nature.* 1960, Sept. 17, v. 187, 1029–30.

OZER, F. L., TRUAX, W. E. & LEVIN, W. C. **Erythroid Hypoplasia associated with Chloramphenicol Therapy.** *Blood.* 1960, July, v. 16, No. 1, 997–1001, 2 figs. [18 refs.]

SOMPOLINSKY, D., YARON, V. & KRONENBERG, Esther. [**The Relative Sensitivity of *Pseudomonas aeruginosa* and other Gram Negative Organisms to Four Tetracyclines. Preliminary Report.**] *Harefuah.* Jerusalem. 1960, Aug. 15, v. 59, No. 4 [in Hebrew 103–4, 1 fig. English summary 105].

The English summary appended to the paper is as follows:—

"Of 85 strains of *Pseudomonas aeruginosa*, 24 strains of *Proteus sp.*, and 19 strains of *Escherichia coli* examined, almost all were more sensitive to demethylchlortetracycline, and less so to oxytetracycline than to the other tetracyclines. No significant difference in the efficacy of chlortetracycline and tetracycline was observed.

"The tetracycline drugs are inactivated in nutrient broth during the first 4–5 days, and then the residual amount seems constant. The inactivation is most radical for chlortetracycline (up to 1/60 of the initial activity), and least so for demethylchlortetracycline (up to 1/4–1/5 of the initial activity).

"By the gradient plate method, increased resistance could be induced to all tetracycline drugs. Adaptation to any of the drugs was followed by cross-resistance to the others. In all cases, strains were obtained more resistant to oxytetracycline than to chlortetracycline. In the case of adaptation to the latter, the cross-resistance to the other tetracyclines was thus 'exaggerated'."

ERMOLIEVA, Z. V. & KHVOLES, A. G. [**The Role of Involutionary Forms of Bacteria in the Estimation of their Susceptibility to Antibiotics**] *Mikrobiologiya.* Moscow. 1960, v. 29, No. 4, 544–7, 3 figs. [In Russian.]

The English summary appended to the paper is as follows:—

"1. A comparative study has been carried out of the susceptibility of bacteria of the colon-typhoid group of tetracycline antibiotics by the serial dilution method and phase contrast microscopy. Both methods yielded closely similar results.

"2. A new principle for estimating of bacterial susceptibility to antibiotics by means of the phase contrast microscope is suggested. It is based on the determination of the minimum concentration of the antibiotic which causes the formation within 4–5 hours of involutionary forms of bacteria."

MÁLEK, P. & KOLC, J. **Penetration of Chlortetracycline into Tissue affected by Pathological Changes.** *Antibiotics & Chemotherapy.* New York. 1960, Aug., v. 10, No. 8, 488–94, 6 figs.

WAISBREN, B. A., KLEINERMAN, L., SKEMP, J. & BRATCHER, G. **Comparative Clinical Effectiveness and Toxicity of Vancomycin, Ristocetin, and Kanamycin.** *Arch. Intern. Med.* 1960, Aug., v. 106, No. 2, 179–93, 1 fig. [21 refs.]

"Ristocetin, vancomycin, and kanamycin were alternately administered to 131 patients with severe staphylococcic infections or bacterial endocarditis. The groups of patients receiving each drug were found to be comparable and the relative clinical effectiveness and toxicity of the three drugs were determined. Each drug was effective in slightly over one-third of the patients studied. No one antibiotic showed marked clinical superiority over the others.

"Significant ototoxicity and nephrotoxicity were found with ristocetin, kanamycin, and vancomycin. In addition, ristocetin caused a high incidence of skin reactions and caused depression of the granulocytic series of white blood cells in some patients.

"The conclusion was reached that ristocetin, kanamycin, and vancomycin are effective antistaphylococcal agents of approximately comparable activity. They all exhibit toxicity greater than that found with the tetracyclines, penicillin, chloramphenicol, and erythromycin. Therefore, ristocetin, vancomycin, and kanamycin should be used only in cases that have not or are not likely to respond to safer antibiotics and in which the condition of the patient justifies the risk of serious toxic reactions."

MOUSTARDIER, G., DULONG DE ROSNAY, C., DUFAU-CASANABE, J., DU PASQUIER, P. & LATRILLE, J. Une méthode chimique de dosage de la kanamycine dans les milieux biologiques. [**A Chemical Method for the Assay of Kanamycin in Biological Media**] *Ann. Inst. Pasteur.* 1960, Sept., v. 99, No. 3, 447–9.

KIRK, Julia M. **The Mode of Action of Actinomycin D.** *Biochim. et Biophys. Acta.* 1960, July 29, v. 42, No. 1, 167–9, 2 figs.

LOWBURY, E. J. L. & LILLY, H. A. **Disinfection of the Hands of Surgeons and Nurses.** *Brit. Med. J.* 1960, May 14, 1445–50, 3 figs. [17 refs.]

This paper describes tests of the efficiency of skin disinfectants performed by 2 principal methods. In the first, after treatment of the hands in various ways, surgical gloves were worn by laboratory personnel for 1 hour or longer. The fingers of one glove had previously been perforated at the tip. At the end of the period of wear, the gloved hands were washed in soap and water and dried on a sterile towel: the finger-tips were then rubbed on glass beads immersed in a sterile fluid to obtain a sample of bacteria escaping through the perforations. Secondly, after removal of the gloves, their interior was washed out with sterile fluid. These fluids (which contained neutralizers for the disinfectants) were then cultivated quantitatively. When the hands had only been "scrubbed up" previously in soap and water, both fluids gave bacterial counts of about 50–300 bacteria per ml. After various antiseptic treatments all counts were much lower: these treatments included immersion in 70% alcohol with or without 0·5% chlorhexidine, the use of hexachlorophane soap both for the scrub and for the previous week, the use of Phisohex in the same way, and the addition of bacitracin and neomycin to the glove powder (the last 2 gave the lowest counts: data only for fluid from the glove interior).

Secondly, nurses regularly using skin disinfectants on their hands were made to wash first in soap and water and then in sterile fluid which was cultivated as before. The exclusive use of hexachlorophane soap produced the lowest counts compared with those from hands of nurses who used ordinary soap: chlorhexidine cream alone or even in combination with the use of hexachlorophane soap gave counts which were less reduced. These findings refer to total bacteria: there were corresponding reductions in the numbers of *Staphylococcus aureus*. All staphylococci proved highly sensitive to hexachlorophane and no nurse's skin became so.

[See also this *Bulletin*, 1958, v. 33, 390; 1959, v. 34, 311.] *L. P. Garrod*

HEICKEN, K. & BELLINGER, H. Die Sterilisation von Catgut mit fasförmigem Äthylenoxyd. **[The Sterilization of Catgut with Gaseous Ethylene Oxide]** *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 179, No. 1, 113–40, 5 figs. [25 refs.]

This paper is from the Robert Koch Institute, Berlin, and is dedicated to Koch on the 50th anniversary of his death. It owes some of its length to introductory reviews of the properties of ethylene oxide, and of the difficulties and methods of sterilizing catgut, and to an extensive description of how to determine the moisture content of catgut, and of how to adjust it in atmospheres of different relative humidities produced by mixtures of sulphuric acid and water in different proportions.

The actual tests were done in a chamber to which a mixture of 10% ethylene oxide and 90% CO_2 was admitted and maintained under a pressure of up to 6 atmospheres at a temperature of 30 or 50°C. Raw catgut was used, of different diameters, in lengths varying from 1 metre to entire coils. They were afterwards cultivated in a cysteine-containing medium which supported the growth of both aerobes and anaerobes. Of the variables studied, the moisture content of the catgut had the most important effect, moisture being evidently necessary to permit diffusion of the ethylene oxide through the catgut. The times required to sterilize No. 3 catgut with a water content of 10, 20, 30 and 40% at a pressure of 6 atmospheres and 30°C. were 480, 120, 30 and 15 minutes respectively. No. 6 catgut required a rather longer time: on the other hand at 50°C. the times were shortened. The effect of varying pressures was also studied. It was shown that whole coils could be sterilized satisfactorily, and furthermore that the gut could be sterilized within sealed "polythene foil" packages, the ethylene oxide diffusing through this material. Numerous tests showed that this treatment does not impair the tensile strength of the gut. *L. P. Garrod*

WELLS, C. & WHITWELL, F. R. **A Small Autoclave in a Large Hospital.** *Lancet.* 1960, Sept. 17, 643–4, 1 chart.

In 1959 a Working Party of the Medical Research Council recommended the use of high-vacuum high-speed steam sterilizers for hospital dressing [this *Bulletin*, 1959, v. 34, 807]. This paper describes the use of such a sterilizer in a general hospital of 650 beds. The sterilizer had a capacity of 3½ cu. ft. (0·1 cu. m.) and for over 3 months it has handled the hospital's weekly requirements of 1,000 dressing drums and 140 glove drums. Previously these were sterilized in a large downward displacement sterilizer of 72 cu. ft. (1·9 cu. m.) capacity. The great output of so small a sterilizer was due to the shortness of the cycle—about 9½ minutes. Tests with Browne's tubes and *Bacillus stearothermophilus* spores were satisfactory in dressing and glove drums. The standard dressing cycle of 135°C. for 3 minutes did not cause excessive damage to gloves and the authors do not consider that a special glove cycle at a lower temperature is necessary. Rubber sheets contained in large drums were not always sterilized and it is suggested that alternatives should be sought.

Although the 3½ cu. ft. chamber was in fact adequate it is suggested that 9 or 10 cu. ft. (0·3 cu. m.) would be the most suitable size as it would allow for expansion of work and permit the operators to work shorter shifts.

[This timely paper will greatly encourage the advocates of the modern high-vacuum sterilizer. It also makes clear that old sterilizers need not be replaced by new ones of comparable size. High-vacuum sterilizers are described in British Standards Specifications 3219 and 3220.] *J. C. Kelsey*

ALLISON, V. D. **Hospital Central Sterile Supply Departments.** *Brit. Med. J.* 1960, Sept. 10, 772–8, 5 figs.

MCNEIL, Ethel, GREENSTEIN, M., STUART, L. S. & GOLDSMITH, Margaret T. **Some Problems involved in the use of Quaternary Ammonium Compounds as Fabric Disinfectants.** *Applied Microbiol.* Baltimore. 1960, May, v. 8, No. 3, 156–9. [12 refs.]

This work was undertaken to elucidate some of the factors involved in fabric disinfection for the prevention of hospital cross-infection. Weighed pieces of gauze and "muslin" (this term is applied in the United States to a much heavier fabric than it denotes in British dressmaking), both as supplied and after "desizing" by 2 different processes, were immersed in solutions of alkyldimethylbenzyl ammonium chloride, and the amount adsorbed was determined. Both adsorbed less after desizing, a fact believed not to be due entirely to starch removal. The concentration of the solution affected the 2 fabrics somewhat differently in regard to the amount adsorbed. Looseness in the weave increases adsorption. In a second series of experiments the capacity of treated fabric to kill bacteria was tested. Pieces weighing 1·5 gm. were placed in 2 ml. broth inoculated with bacteria of 4 species, and incubated for 4 hours, when 25 ml. thioglycollate broth was added and incubation continued. The frequency of subsequent growth in multiple tests is stated for 7 different contents of disinfectant, varying from 2 to 22 mgm., for both fabrics. Staphylococci and 2 other rather strangely chosen Gram-positive organisms were usually [apparently] killed by the smaller amounts of disinfectant and always by the higher: *Proteus mirabilis*, as might be expected, often survived. [These experiments appear to be vitiated by the absence of a

satisfactory neutralizer: the authors speak of these preparations being "sterilized", but in the continued presence of the disinfectant they may only represent inhibition of growth. No attempt is described to determine how much of the disinfectant is liberated when treated fabric is immersed.] *L. P. Garrod*

SPINER, D. R. & HOFFMAN, R. K. **Method for Disinfecting Large Enclosures with β-Propiolactone Vapor.** *Applied Microbiol.* Baltimore. 1960, May, v. 8, No. 3, 152–5.

These workers from the U.S. Army Chemical Corps, Fort Detrick, first define the properties desirable in a gaseous disinfectant, which they claim are satisfied best by propiolactone, and then the conditions for the use of this substance. The room or building must be sealed, and all the doors, drawers and cupboards opened: the temperature should be 24°C. and the humidity at least 70%, to be attained by spraying water if necessary; finally β-propiolactone is sprayed in it, using a fine spray so that there is not much "fall-out" of droplets, in an amount sufficient to give a concentration of 2–4 mgm. per litre of air. In practice the theoretical amount must be exceeded, particularly if "highly absorptive" material is present, such as "rugs, drapes, overstuffed furniture": 1 gallon per 12,000 cu. ft. is suggested for such a room and 1 gallon per 16,000 cu. ft. for a laboratory. The vapour is allowed to act for 2 hours, and the room or building is then ventilated.

Particulars are given of what was actually done in a two-storey army barrack, a furnished hospital day-room, an army hospital ward and an animal house. In each of these, numerous surfaces were previously contaminated with bacterial spores and subsequently cultivated, usually with negative results.

Precautions for the safety of operators are defined: those entering a treated area, *e.g.* to open windows at the end of a disinfection period, should wear a gas mask containing charcoal, and washable outer clothing which is then removed. [The authors do not seem to think that the inhalation of a tolerable concentration, which is about 0·1 mgm. per litre, or transient contact with the skin, can be harmful. Yet they quote others who have shown that β-propiolactone is carcinogenic in rats and mice, and conclude that "repeated exposure to subirritating doses of BPL vapor should be avoided". Can it be avoided by an operative who has charge of this process in the event of its general adoption?] *L. P. Garrod*

GILLISSEN, G. Entfernung von Mikroorganismen mittels Ionenaustauscher. **[The Removal of Micro-organisms by means of Ion-Exchange Materials]** *Gesundheits-Ingenieur.* 1960, July 11, v. 81, No. 7, 207–10.

Suspensions of *Escherichia coli* were passed through ion-exchange columns and survivors were enumerated by counting colonies on membrane filters. The organisms passed freely through a cationic exchange column, but were retained in 2 of anionic type: (the Tables of results are difficult to understand, but it seems that up to about 99·9% of the organisms were retained in some of the experiments). Among the findings in various subsidiary experiments were that efficiency of bacterial removal is diminished by increased density of the suspension but not by repeated use of the column (one regenerated with NaOH improved in efficiency), and that the electric charge is important, since treatment of the column with an "antistatic" deprived it of its power to retain bacteria. *L. P. Garrod*

BACTERIA

The order in this section is:—**Cocci; Donovania; Mycobacterium; Corynebacterium; Haemophilus; Pseudomonas; Pfeifferella; Enteric Organisms; Brucella; Pasteurella; Bacillus; Anaerobes; Spirochaetes; Erysipelothrix; Listeria; Others.**

ROSENBLUM, E. D. & DOWELL, C. E. **Lysogeny and Bacteriophage Typing in Coagulase Positive Staphylococci.** *J. Infect. Dis.* 1960, May–June, v. 106, No. 3, 297–303. [15 refs.]

96 strains of coagulase-positive staphylococci were tested by cross-culture tests for lysogenicity and for sensitivity to the temperate phages carried by other strains from the collection. Altogether 82 strains were found to be lysogenic. Their phages were active principally against other strains of the same phage sensitivity group, as determined by typing with the standard set of phages. Lysogeny can therefore be used as an aid in the classification of staphylococci. On this basis there was some suggestion that phages 42B, 47C and 81 ought to be classed with Group I, and phage 187 with Group II. *R. E. O. Williams*

GRÜN, L. & PULVERER, G. Ergebnisse einer Differenzierung von Staphylokokken des Phagtyps "80". **[The Differentiation of Staphylococci of Phage type "80"]** *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 146, No. 5, 385–96. [27 refs.]

67 strains of *Staphylococcus aureus* of phage-type 80 were tested for lipase, haemolysin, fibrinolysin and pigment production, action on mannitol and urea, antibiotic sensitivity, and serological type. All produced haemolysin, fibrinolysin and a golden pigment, and all but 2 or 3 attacked mannitol and urea. 36 produced lipase. 13 strains were resistant to penicillin alone and 45 to penicillin and streptomycin while the other 9 strains had various resistance patterns. 63 strains had the antigenic formula *abcehik*; 42 were also agglutinated by the *f* serum. [See OEDING and

WILLIAMS, this *Bulletin*, 1959, v. 34, 573.] It is concluded, from consideration of the differences in lipase, antibiogram and serology, that strains lysed by phage 80 alone do not necessarily all belong to one type.

R. E. O. Williams

NESTORESCO, N., POPOVICI, Marcela & ALEXENCO, Ecaterina. Les rapports entre la résistance des staphylocoques aux antibiotiques et leur sensibilité à l'action des bactériophages. [**Investigations concerning the Relationship between the Resistance of Staphylococci, as induced *in vitro* by means of Antibiotics, and their Sensitivity to Specific Phages**] *Arch. Roumaines Path. Expér et Microbiol.* 1960, Mar., v. 19, No. 1, 69–84, 12 figs. [34 refs.]

19 strains of *Staph. aureus* were passed repeatedly in the presence of various antibodies and the increase in resistance determined. This increase was no more than 2-fold for aureomycin, and 4–80 fold for penicillin and chloramphenicol; increases of up to 100,000-fold were observed with streptomycin, and 40,000-fold for erythromycin. There were no changes in phage types.

R. E. O. Williams

QUIE, P. G., COLLIN, May & CARDLE, J. B. **Neomycin-Resistant Staphylccocci.** *Lancet.* 1960, July 16, 124–6, 1 fig. [11 refs.]

In a Minneapolis hospital the first strain of a coagulase-positive staphylococcus found to be resistant to neomycin (in a test with a paper disc containing 5 μgm.) was isolated from a patient in February 1959. By December 1959 resistant strains had been isolated from 144 patients; in all 20·8% of the 1,248 staphylococci tested in 1959 were resistant. Of the 144 patients, 58 had had neomycin treatment. 12 strains were all lysed by phage 54 used at 100 times the critical test dilution. There was complete cross-resistance between neomycin and kanamycin [this *Bulletin*, 1959, v. 34, 655].

R. E. O. Williams

THOFERN, E. & BRANDIS, H. Über den Einfluss des Protamins auf den Oxydationsstoffwechsel von *Staphylococcus aureus* und über die Protamin-bedingte Abtötung der Bakterien. [**On the Influence of Protamine on the Oxidative Metabolism of *Staphylococcus aureus* and on the Bactericidal Effect of Protamine**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 179, No. 4, 483–90, 5 figs.

GREENBERG, L. & COOPER, Margaret Y. **Polyvalent Somatic Antigen for the Prevention of Staphylococcal Infection.** *Canadian Med. Ass. J.* 1960, July 23, v. 83, No. 4, 143–7, 1 fig.

Hamsters and rabbits were imunized either with a vaccine prepared from whole, heat-killed, staphylococci, or with a lysate prepared from similar cells by treatment with the enzyme preparation Dornase. The latter is referred to as the "somatic" antigen vaccine. The animals were given a single subcutaneous and intracutaneous injection and challenged 2 weeks later by the intravenous or intracutaneous routes. The results are not presented in full, but it was found that the somatic vaccine protected against a wider variety of strains than the whole cell vaccine; however, with neither was a vaccine prepared from a single strain able to induce protection against all the challenge strains used. A polyvalent somatic antigen incorporating 5 strains of different phage types was therefore developed and found to have a wide protective action. An agglutination test was developed in which the serum was mixed with a latex particle suspension previously treated with the somatic antigen. Rabbits with a serum agglutination titre of 1 in 600 or more proved resistant to intravenous challenge, but were not necessarily resistant to intradermal challenge; for the latter intradermal inoculation of vaccine had to be employed. Antihaemolysin was not developed in response to the vaccines used.

[Further detailed results of these studies will be awaited with great interest and in particular the relation of the lesions produced by the challenge dose to those produced by injections of toxin.] *R. E. O. Williams*

HINKLE, Nancy H., PARTIN, J. & WEST, C. D. **Nephropathy in Mice after Exposure to Group A, Type 12 Streptococci.** *J. Lab. & Clin. Med.* 1960, Aug., v. 56, No. 2, 265–76, 7 figs. [13 refs.]

BRIDSON, E. Y. & BROWN, Jean. **Tyramine-Producing Streptccocci in Neonatal Diarrhoea.** *J. Clin. Path.* 1960, May, v. 13, No. 3, 195–8.

In the stools of 15 newborn babies in one nursery, who were suffering from diarrhoea and 2 of whom died, a β-haemolytic streptococcus was found predominant. The streptococcus belonged to group D and was classed as *Str. fæcalis* var. *zymogenes.* Subsequently 81 strains of similar streptococci were isolated from 347 healthy babies. No difference could be found in the tyrosine decarboxylase activity of the strains from the ill and healthy babies. *R. E. O. Williams*

SKORKOVSKÝ, B. Rhodanidtest zur Differenzierung von Enterokokken. [**Thiocyanate Test for Differentiation of Enterococci**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 178, No. 4, 491–5. [10 refs.]

Potassium thiocyanate inhibits the growth of greening and haemolytic streptococci in broth in a concentration of 1–·5%; 4–·5% is needed to inhibit the growth of enterococci or (on the basis of 3 strains) "milk streptococci". A medium containing 2·25% potassium thiocyanate is suggested as an indicator medium.

R. E. O. Williams

GUTHOF, O. Zur Frage der Identität pathogener vergrünender Streptokokken mit den "normalen Mundstreptokokken". [**The Identity of Pathogenic Greening Streptococci with Normal Mouth Streptococci**] *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 146, No. 5, 425–32. [24 refs.]

203 strains of streptococci from the mouths of normal children were examined by a number of physiological tests to discover the frequency of recognized pathogenic varieties; 1 typical *Str. sanguis* and 3 dextran-forming strains lacking some of the characteristics of *Str. sanguis* were found. There were 24 strains of *Str. salivarius* (*hominis*) and 3 *Aerococcus viridans*. The rest of the strains belonged, in general, to the *mitis* group. Sensitivity to Optochin, Bacitracin and Furacin was found to be a useful test for distinguishing *Aerococcus* viridans and *Str. milleri* from enterococci and *mitis* streptococci, *Aerococci* are sensitive to bacitracin while enterococci are not; *Str. milleri* is resistant to all 3 drugs while all *mitis* strains are sensitive, at least, to Furacin.

R. E. O. Williams

LUND, Erna. **Laboratory Diagnosis of *Pneumococcus* Infections.** *Bull. World Health Organization.* Geneva. 1960, v. 23, No. 1, 5–13. [19 refs.]

This paper summarizes methods for the identification and typing of pneumococci, for the production of typing sera, and for the recognition of type-specific antibodies in convalescence. There is a summary of the antigenic formulae of the capsules in the 47 types recognized by Danish workers and a concordance of the American and Danish typing schemes. *R. E. O. Williams*

MASAMUNE, Y., ABE, M. & MIZUNO, D. **A Stabilizing Effect of Hemoglobin on the *Pneumococcus* Transformation.** *Japanese J. Med. Sci. & Biol.* 1960, Apr., v. 13, Nos. 1/2, 23–31, 3 figs. [10 refs.]

MIETH, H. Untersuchungen über das Vorkommen von Enterokokken bei Tieren und Menschen. I. Mitteilung: Ihr Vorkommen im Darm von gesunden Schlachtschweinen. [**Experiments on the Presence of Enterococci in Animals and Humans. Part I: Their Presence in the Intestines of Healthy Pigs**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 179, No. 4, 456–82. [32 refs.]

TARSHIS, M. S. **A Direct Qualitative Micro-Niacin Test for differentiating Human Tubercle Bacilli from other Mycobacteria. A Modified Procedure.** *Amer. Rev. Respiratory Dis.* 1960, July, v. 82, No. 1, 82–90, 2 figs. [26 refs.]

As a result of an investigation into the niacin test the author recommends that for this test the mycobacteria be grown on either of 2 media which he developed after many trials. Both of these media contain Tween 80 0·2 gm., K_2SO_4 0·5 gm., Mg citrate 1·5 gm., KH_2PO_4 5·0 gm. asparagine 5·0 gm., agar 15 gm., and glycerol, 20 ml., and in the Tween-albumin [TAN] medium these ingredients are dissolved in 900 ml. of distilled water and 100 ml. of water containing bovine albumin fraction V, 5 gm., dextrose 7·5 gm. and NaCl 0·85 gm., are added. In the Tween-charcoal [TCN] medium, Norit A carbon, 1·0 gm. and dextrose 7·5 gm., are added to the ingredients and dissolved in 1,000 ml. of distilled water. The *p*H value of both media is 6·6.

On these media sufficient growth is usually present after 7–10 days, and then 2–10 drops of water, the number depending on the quantity of moisture in the tube, are added by means of an expendable plastic straw. After the tube has been in the horizontal position for 5 minutes, with the water flooding the growth, 4 drops of the extract are removed into a serological tube and sterilized for 15 minutes at 15 lb. steam pressure. The test for niacin can then be done on a well-plate or in another tube; to 2 drops of the extract are added 1 drop 4% aniline in ethanol and 1 drop of 10% cyanogen bromide in water and the result is read within 2 minutes by means of a reflected fluorescent light source. A distinct yellow colouring signifies a positive reaction.

The advantages claimed for the method are that the sterilizing of the culture before making the test reduces the risk of infection and the use of the small quantities of reagents minimizes the toxicity and unpleasantness of the cyanogen bromide. Also, as an alternative method the extract can be absorbed on to a cotton wool swab and the reagents added also by absorption, but with this method weak reactions may be more difficult to read.

Of 22 strains of mycobacteria examined, only the 9 strains of human tubercle bacilli gave positive reactions.

S. R. M. Bushby

SCHMIEDEL, A. Erfahrungen mit der Typendifferenzierung von Tuberkelbakterien in der Agar-hohe-Schicht Kultur. [**Experiences of Type Differentiation among Tubercle Bacilli in deep Agar tube Culture**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1960, May, v. 6, No. 5, 303–10, 3 figs. [33 refs.]

The author has investigated the value of a test introduced by LEBEK in 1958 [this *Bulletin*, 1959, v. 34, 570, 667] in which bovine and human tubercle bacilli are differentiated by their oxygen requirement. For this purpose a tube of 2% "Sauton agar" with 10% serum and 6% glycerine is heavily inoculated with a well-dispersed suspension of the bacilli under investigation. When this is allowed to set and incubated the human strains grow freely on the surface whereas the bovine strains give growth in depth with an opaque disc-like zone of maximum growth some 10 or 20 mm. below the surface. Experimental evidence is recorded to prove that this type of growth depends on the microaerophilic quality of the bovine tubercle bacillus which gives its heaviest growth in the zone of optimum O_2 concentration. This method is helpful in the differentiation of normal bovine and human strains of dysgonic human

strains and isoniazid-resistant strains. It does not help in the differentiation of bovine strains which are naturally eugonic or old bovine strains which have become eugonic on prolonged sub-culture, nor the BCG strain.

Observations of 128 human and 156 bovine strains have been tested and the differentiation of bovine strains from isoniazid-resistant human strains tending to dysgonic growth were satisfactory.

It is suggested that this test may serve as an economical substitute for the differential rabbit and guineapig pathogenicity test. *J. W. McLeod*

Hsu, H. S. & Kapral, F. A. **The Suppressed Multiplication of Tubercle Bacilli within Macrophages derived from Triiodothyronine-Treated Guinea Pigs.** *Amer. Rev. Respiratory Dis.* 1960, June, v. 81, No. 6, 881–7, 2 figs. [17 refs.]

Lurie *et al.* [this *Bulletin*, 1959, v. 34, 665] suggested that hyperthyroidism alters the physiological activity of phagocytes and thus enhances the suppression of intracellular multiplication of tubercle bacilli; the purpose of the present study was, in part, to test this suggestion.

Macrophages were obtained from peritoneal exudates of guineapigs that were either normal or in a hyperthyroid state due to a daily injection of 10 μgm. L–3:5:3′–triiodothyronine [the active principle of the thyroid gland], and after the cells had been allowed to ingest tubercle bacilli they were transferred to coverslips. The coverslips were then placed in culture medium consisting of 20% guineapig serum, 65% Hanks solution and 15% sodium bicarbonate solution (1·4%), containing in addition to nystatin and penicillin, 5 μgm. streptomycin per ml. to inhibit extracellular growth of the tubercle bacilli. At chosen intervals the average number of viable bacilli per cell was calculated by removing pairs of coverslips from the culture medium, enumerating the total number of macrophages on one and determining the culturable intracellular bacilli on the other; for the latter count the macrophages were first disrupted by immersion in 1% sodium deoxycholate and the viable counts then made on Dubos medium +2% agar.

2 strains of H37Rv were used; one, H37Rv–P, was somewhat attenuated, and the other H37Rv–S was virulent. The results showed that with H37Rv–P there was a lag phase of 4–5 days' duration, followed in the normal macrophages by a phase of growth lasting 2–3 days during which there was an approximately 4–fold increase, but in macrophages from the hyperthyroid animals this growth was somewhat suppressed; with this strain there was no further increase in the number of bacilli after 7 days' incubation. With H37Rv–S there was little or no lag phase in the normal macrophages and the bacilli continued to multiply for 9 days with a generation time of 2–3 days, whereas in the macrophages from the treated animals there was a lag phase of 2 days followed by slow multiplication with a generation time of 5 or more days.

The authors conclude that the results confirm that there is a cellular resistance which can be induced by administration of a naturally occurring single hormone. *S. R. M. Bushby*

Soru, Eugenia, Istrati, Maria, Sculptoreanu, Judith & Paraschivesco, Maria. Étude enzymologique comparative du *Mycobacterium tuberculosis* BCG et ses variantes résistantes à la streptomycine, PAS et INH. I. Transaminases. II. Enzymes d'oxydoréduction. [**A Comparative Enzymological Study of *Mycobacterium tuberculosis* BCG and of its Streptomycin-, PAS-, and INH-Resistant Variants. I. Transaminases. II. A Study of Respiration and of Oxido-reducing Enzymes**] *Arch. Roumaines Path. Exper. et Microbiol.* 1960, June, v. 19, No. 2, 189–99, 6 figs. [19 refs.]

Youmans, Anne S. & Youmans, G. P. **The Production of "Anti-Isoniazid" Substance by Isoniazid-Susceptible, Isoniazid-Resistant, and Unclassified Strains of Mycobacteria.** *Amer. Rev. Respiratory Dis.* 1960, June, v. 81, No. 6, 929–31. [Refs. in footnotes.]

The authors had previously reported [this *Bulletin*, 1956, v. 31, 78, 1159] that extracts of tubercle bacilli inactivated isoniazid *in vitro* and reversed the activity of the drug in turberculous mice; also an isoniazid-resistant variant of H37Rv was shown to produce less of this enzyme-like substance than did the parent strain.

In the present study, using filtrates of 6 unclassified strains of mycobacteria, 10 isoniazid-resistant strains, 15 recently isolated isoniazid-susceptible strains of tubercle bacilli, H37Rv and H37RaN, the authors show that the unclassified and drug-susceptible strains produced a significantly larger amount of anti-isoniazid substance than did the resistant strains and H37RaN. There was no relationship between the production of anti-isoniazid and the catalase activity of the resistant strains, but more anti-isoniazid was produced by resistant strains isolated from man than from strains which developed resistance *in vitro* or in the rabbit. The presence of isoniazid in the culture medium did not increase production of anti-isoniazid.

The production of this anti-isoniazid substance is contrasted with that of penicillinase; penicillin-susceptible strains of staphylococci do not appear to produce penicillinase, whereas resistant strains do produce it [*ibid.*, 1945, v. 20, 100], and moreover, penicillinase has been shown to be an adaptive enzyme [*ibid.*, 1957, v. 32, 996] while anti-isoniazid apparently is not.

S. R. M. Bushby

Youmans, G. P., Youmans, Anne S. & Parlett, R. **The Incidence of Hypersensitivity to Mammalian and Battey PPD in Medical and Dental Students.** *Amer. Rev. Respiratory Dis.* 1960, July, v. 82, No. 1, 114–16. [Refs. in footnotes.]

"One hundred and seventy-eight medical and dental students at Northwestern University were skin-tested with 5 TU of PPD prepared from the unclassified Battey Mycobacterium and with 5 TU of PPD prepared from *M. tuberculosis*. Fifty-four students (30.3 per cent) gave reactions; 21 (11.8 per cent) reacted to both tuberculins, 27 (15.2 per cent) reacted only to PPD-B, and 6 (3.4 per cent) only to PPD-S."

ATWELL, R. J. & PRATT, P. C. **Unclassified Mycobacteria in the Gastric Contents of Healthy Personnel and of Patients of a Tuberculosis Hospital.** *Amer. Rev. Respiratory Dis.* 1960, June, v. 81, No. 6, 888–92. [19 refs.]

From March to July 1957, single gastric aspirations were taken by means of a Levin tube from 112 employees of the Ohio tuberculosis hospital and 101 samples were taken from 30 patients. The tube was cooled in ice and lubricated with sterile mineral oil; it was passed through the nose and into the stomach. A year later the procedure was repeated twice on 87 of the employees, except that the tubes were cooled unwrapped in a freezer and a sterile lubricant jelly was used. Also in 1958, 40 patients had 184 gastric samples taken by the original method, and 87 had 296 samples taken by the modified one. The specimens were treated with caustic soda, inoculated onto Löwenstein medium and injected into guineapigs; smears were also examined for acid-fast bacilli. In 1958 nasal smears were also examined.

The results of the cultures were:

	1957		1958		
				Patients	
	Employees	Patients	Employees	Old method	New method
% Positive smear	1·8	—	10·3	—	—
% Positive culture	18·8	9·9	2·3	9·2	2·7
% Persons with positive culture	18·8	26·7	4·6	27·5	9·2

Of the 22 positive cultures in 1957 from the employees, 18 were orange-scotochromogens, 3 were non-photochromogens, and 1 was a virulent tubercle bacillus. (This strain was from a person without evidence of tuberculosis.) The 10 positive cultures from the patients of this period, were slow-growing orange-scotochromogens, and all the positive cultures of 1958 were of this same type. None of these unclassified bacilli were pathogenic to the guineapig.

All the nasal smears from the employees were negative and attempts to grow the bacilli from ice, tap water or mineral oil were unsuccessful.

The results, especially those from the patients, are further analysed and the authors conclude that the incidence of these organisms in both employees and tuberculous patients was reduced by refining the technique of aspiration, and that the data indicated a sporadic inconsistent source of unclassified mycobacteria, unrelated to tuberculosis or chemotherapy.

S. R. M. Bushby

SMITH, N. **The "Dassie" Bacillus.** *Tubercle.* 1960, June, v. 41, No. 3, 203–12, 4 figs.

This mycobacterium was originally isolated from an epithelioid granuloma in the lungs of the rodent common to South Africa, *Procavia capensis* or "Dassie", by WAGNER *et al.* (*Nature*, 1958, v. 181, 284). The organism appeared to resemble the vole bacillus but although it produced caseation of lymph glands when injected into other Dassies, it was of very low virulence to rabbits, guineapigs, mice and various other veldt rodents.

The present author has examined the strain and finds that morphologically it resembles the vole bacillus by being very pleomorphic in lesions and the curved forms tending to form spirals or hooks, but differing by being more granular. It is strongly acid-fast.

Culturally it was a strict aerobe that takes 6 weeks for the primary growth to develop on Dorset egg medium, but it grew more rapidly in secondary cultures; on this medium the growth was almost white, rough and friable. It could be readily adapted to grow in Dubos medium, and experiments with the basal medium showed that 0·1% sodium glutamate with 0·2% asparagine was preferable to casein digest as the source of nitrogen.

The bacillus was slightly more sensitive to streptomycin and isoniazid than is H37Rv, and it survived exposure to 10% NaOH and H_2SO_4 for 30 minutes and to 0·5% phenol for 24 hours; it was killed by heating for 30 minutes at 60°C. but not at 55°C.

S. R. M. Bushby

DE SOUZA, P. R., DE AZEVEDO, M. P. & DE CASTRO, Maria P. *Mycobacterium leprae* em cultura de tecido. [*M. leprae* **in Tissue Culture**] *Rev. Assoc. Med. Brasileira.* 1959, Dec., v. 5, No. 6, 408–12, 6 coloured figs. on pl. [19 refs.] English summary.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 1270.]

REES, R. J. W., VALENTINE, R. C. & WONG, P. C. **Application of Quantitative Electron Microscopy to the Study of** *Mycobacterium lepraemurium* **and** *M. leprae*. *J. General Microbiol.* 1960, Apr., v. 22, No. 2, 443–57, 9 figs. on 2 pls. & 1 text fig. [25 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 1275.]

SHEPARD, C. C. **Acid-Fast Bacilli in Nasal Excretions in Leprosy, and Results of Inoculation of Mice.** *Amer. J. Hyg.* 1960, Mar., v. 71, No. 2, 147–57. [11 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 1269.]

THURSTON, J. R., HAWKINS, Jean E. & STEENKEN, W., Jr. **The Effect of Filtration of Biologic Products. I. Influence on the Serologic Activity of Old Tuberculin.** *Amer. Rev. Respiratory Dis.* 1960, July, v. 82, No. 1, 77–81.

"Seitz filtration of Trudeau OT (TOT) removes the erythrocyte-sensitizing substance without altering the capacity of the TOT to react in gel precipitin tests or to inhibit hemagglutination or hemolytic tests. The adsorptive capacity of the Seitz filter is limited.

"Millipore (HA) and fritted glass (UF) filters had only a slight effect on the erythrocyte-sensitizing-substance content of small volumes of TOT 1:15."

EDWARDS, D. C. **The Growth and Toxin Production of *Corynebacterium diphtheriae* in Submerged Culture.** *J. General Microbiol.* 1960, June, v. 22, No. 3, 698–704, 3 figs. [24 refs.]

A method of culture in bulk in tanks in which the medium was kept in continuous agitation and frothing controlled by an "anti-foam" preparation and a regulated current of air passed over the surface was used. In a medium of papain digest of beef with yeast derivative, acetic acid and maltose the correlation of toxin production to other metabolic activities was investigated in the above conditions.

Toxin estimations were only made by the flocculation methods introduced by RAMON and by GLENNY and OKELL.

The chief findings were that growth preceeded toxin formation by about 12 hours (there was no lag period in the conditions of inoculation and growth) but there was no close correlation between rate of growth and rate of toxin production. There was no demonstrable correlation between maltose metabolism or catalase formation and toxin production and although in 2 instances toxin and porphyrin production corresponded, in a third they diverged. *J. W. McLeod*

EDWARDS, D. C. & SEAMER, P. A. **The Uptake of Iron by *Corynebacterium diphtheriae* growing in Submerged Culture.** *J. General Microbiol.* 1960, June, v. 22, No. 3, 705–12, 2 figs. [11 refs.]

The authors proceeded to reinvestigate the influence of iron content on growth and toxin production by *Corynebacterium diphtheriae* in cultures produced under the conditions described by Edwards [see above].

Iron concentrations ranging from 0·18 μgm./ml. to 3·1 μgm./ml. were produced in the medium. There was no evidence that the rate of growth was seriously affected by the iron-content and practically all the iron was taken up by the bacteria within 48 hours in the range of concentrations observed. There was no evidence that the oxygen uptake varied on account of the variation in iron uptake by the bacteria. There was a maximum toxin production with the lowest addition of iron *i.e.* 270 Lf./ml. and this fell steadily till, with 3·1 mgm./ml., there was none. This effect was due to a later start of toxin production in the cultures containing more iron and in this respect ferrous was more effective than ferric iron.

Thus, although a phenomenon similar to that described by PAPPENHEIMER [this *Bulletin*, 1948, v. 23, 356] was observed, the sensitivity of toxin production to iron content of medium was much less than in the simpler media used by Pappenheimer in his experiments, a limiting concentration was observed at 0·6 μgm./ml., whereas in these the corresponding value was >1·8 μgm./ml. The ratio of iron to dry weight of bacteria found inhibitory of toxin production was 0·14–0·16 μgm. iron/mgm. dry weight. *J. W. McLeod*

ALBERTI, Silvana & ORTALI, V. Su di un nuovo terreno d'arricchimento per il *Corynebacterium diphtheriae.* [**A New Enrichment Medium for *Corynebacterium diphtheriae***] *Rendiconti Istituto Superiore di Sanità.* Rome. 1960, v. 23, Pt. 2, 146–52. [14 refs.] English summary (5 lines).

This fluid medium depends on a very high concentration of peptone, 6%, and a trace of cystine for its capacity to promote the growth of all corynebacteria, and on its content of $CuSO_4$, $CaCl_2$ and Na azide for the inhibition of diphtheroids and other contaminants likely to appear in cultures from cases of diphtheria or carriers of the *C. diphtheriae.*

In a series of 55 patients from whom swabs had been examined at the same time by the usual methods in the Laboratory of Hygiene at Rome with 10 positive results, the enrichment method described gave 3 additional positives, but 3 of the Hygiene, Laboratory positives were found negative. *J. W. McLeod*

YONEDA, M. & ISHIHARA, H. **Studies on the Iron-Binding Site of Diphtheria Bacilli. 1. Quantitative Binding of Iron by Iron-Deficient Cells of a Toxinogenic Strain of *Corynebacterium diphtheriae.* *Biken's J.*** Osaka. 1960, Mar., v. 3, No. 1, 11–26, 5 figs. [16 refs.]

NARBUTOWICZ, Barbara. Wpływ digitoniny na czestotliwośc lizogenizacji maczugowców błonicy. [**The Effect of Digitonin on the Frequency of Lysogenization of *Corynebacterium diphtheriae***] *Med. Dośw. i Mikrob.* Warsaw. 1960, v. 12, No. 3, 231–4. [11 refs.]

The English summary appended to the paper is as follows:—

"It was stated that digitonin in concentration of 2.5 per cent, increased the frequency of lysogenisation and the lysogenic conversion to toxigenicity of *Corynebacterium diphtheriae.* Since digitonin is known to interfere specifically with lipids its effect on the process of lysogenisation, recorded in the present study, can be related to the ability of interacting with lipids or lipid complexes synthetized in the vegetative phase of phage reproduction."

IAGNIATINSKAIA, Y. G. **Toxigenicity of *Corynebacterium diphtheriae* Strains isolated from Patients and Carriers.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 9, 25–8. [Translated from Russian.]

Apart from the corroboration of the work of others on the reliability of the "*in vitro*" test for toxin production by *Corynebacterium diphtheriae* introduced by OUCHTERLONY [this *Bulletin*, 1949, v. 24, 901] and by ELEK [*ibid.*, 1948, v. 23, 445], the most important practical point made in this communication is that the test can be used with mixed cultures. [Unfortunately the paragraph in the translation which states the grounds for this conclusion is incomprehensible.]

Apart from this the communication indicates that in the vicinity of Saratov there was a predominance of *gravis* strains in recent years. Among 416 strains isolated, 321 *gravis* and 95 *mitis*, 82·2% of the former and 8·4% of the latter were found to be toxigenic.

J. W. McLeod

YONEDA, M., ISHIHARA, H. & OKUDA, M. **Studies on the Extracellular Protein of a Toxinogenic Strain of *Corynebacterium diphtheriae*. I. Effect of Iron on the Release on the Extracellular Protein.** *Biken's J.* Osaka. 1960, Mar., v. 3, No. 1, 77–86. [16 refs.]

KATO, I., NAKAMURA, H., UCHIDA, T., KOYAMA, J. & KATSURA, T. **Purification of Diphtheria Toxin. II. The Isolation of Crystalline Toxin-Protein and some of its Properties.** *Japanese J. Exper. Med.* 1960, Apr., v. 30, No. 2, 129–45, 8 figs. [48 refs.]

By using a preliminary fractionation by precipitation at 50–55% saturation with ammonium sulphate and following the method of Pappenheimer, a relatively pure toxin containing 2,000–2,500 Lf per mgm. N was obtained. And starch block electrophoresis yielded a product from which crystals were separated with an activity of 3,200–3,300 Lf units per mgm. protein nitrogen. This appeared to be homogenous on testing by electrophoresis, by sedimentation and by solubility. Deoxyribonuclease and antigenic protein resistant to heat denaturation such as POPE [this *Bulletin*, 1957, v. 32, 1098; 1958, v. 33, 877] found in some preparations of crystalline diphtheria toxin were not detected.

J. W. McLeod

BRANHAM, Sara E., HIATT, C. W. & RIGGS, D. B. **Properties of Diphtheria Antitoxins produced in Guinea-Pigs with Use of Freund's Adjuvant.** *Proc. Soc. Exper. Biol. & Med.* 1960, July, v. 104, No. 3, 484–6, 1 fig.

Immunizing guineapigs with toxoid from PW.8 and from two *gravis* strains antibodies were obtained which behaved like those of the rabbit rather than those of the horse, *i.e.* flocculation curves were obtained which diminished with excess of antigen but not with excess of antibody.

J. W. McLeod

BERENBAUM, M. C., UNGAR, J. & STEVENS, W. K. **Intracranial Infection of Mice with *Bordetella pertussis*.** *J. General Microbiol.* 1960, Apr., v. 22, No. 2, 313–22, 12 figs. on 2 pls. & 2 text figs. [16 refs.]

Unprotected mice and those protected by 1,000 x 10^6 formolized or ultra-violet irradiated *Bordetella* [*Haemophilus*] *pertussis* organisms given intra-peritoneally 2 weeks before were challenged with 5,000 living *Bordetella pertussis* given intracranially either *via* the parietal bone or through the foramen magnum. The results were independent of the route of inoculation.

The mice were killed at intervals, the lesions noted, sections of brain cut and counts made of *Bordetella pertussis* in brain, cranial cavity washings, blood, liver, spleen, and lungs.

Indian ink revealed that injected material spread throughout the subarachnoid space and ventricles and also along the sheaths of nerves II and VIII: penetration of the veins of the nasal septum, turbinates, and dural venous sinuses was observed.

In protected mice the challenging dose became undemonstrable in the first 24 hours, later increased one hundredfold and was eliminated by the fifth day. The mice were not obviously ill but a meningeal polymorphonuclear reaction due to the suspending fluid appeared, became increasingly mononuclear, and occasionally left residual granulomata superficial and deep to the IVth ventricle.

Unprotected mice became ill after 4 days with signs of meningeal irritation and brain damage and all were dead by the eighth day. The bacteriological and histological findings in the first 24 hours were practically identical with those in the protected mice. Thereafter bacterial multiplication was progressive until death and was restricted to the ciliated ependymal epithelium. There was no bacterial invasion of brain substance and no extra-cranial spread unless heavier inocula were used. By the third day purulent meningitis was established and the choroid plexus, perivascular spaces and cerebral substance became infiltrated with polymorphs. Later widespread haemorrhages were evident and by the sixth day liquefactive necrosis, ventricular distension and hydrocephalus were found and death soon followed.

Stewart Fletcher

BONCIU, C., FAUR, Yvonne, ANDREESCO-TIGOIU, Viorica & IONESCO, Honorina. 'Infection expérimentale par voie aérienne (aérosols) de la souris avec le B. pertussis. [**Histological Lesions and their Dynamics in Mice infected with *Bordetella pertussis* by Aerial Route (Aerosols)**] *Arch. Roumaines Path. Expér. et Microbiol.* 1958, Sept.–Dec., v. 17, Nos. 3/4, 533–44, 8 figs. [17 refs.]

The authors find that infection of mice by a pertussis aerosol causes the following lesions:—peribronchial, perivascular and septal infiltrative lesions, haemorrhagic lesions, lesions of acute alveolitis, interstitial pneumonia, pneumonic and bronchopneumonic foci, abscesses, exudative pleuritis, emphysema, atelectasis, and bronciectasis. Other organs are also infected and tracheobronchial acute adenitis and peri-adenitis, acute hepatitis, a reactive haemorrhagic spleen, a septic spleen, acute degenerative nephritis, acute myocarditis, meningeal reactions and encephalitis may also be found.

The lesions develop in the following order:—in the lung, peribronchial and later perivascular and septal infiltration is followed by endo-alveolar lesions developing into pneumonic foci and abscesses; endobronchial lesions evolving towards suppurative bronchitis are the last to appear. The course of hepatic and renal lesions is similar to that of pulmonary infiltrative lesions, while

splenic and lymphonodular lesions follow the course of endoaleolar and endobronchial lesions. Regression of the pulmonary lesions occurs in the inverse order, *i.e.* endoalveolar and endobronchial lesions are the first to subside, followed later on by septal, perivascular and peribronchial lesions.

In mice infected by the endonasal route, similar lesions occur with the exception of endobronchial lesions, which set in at an earlier period (at the same time as interstitial and alveolar infiltration) and are advanced from the beginning.

It appears that the histological lesions occurring in mice after infection with an aerosol of *Bordetella pertussis* are so similar to those occurring in children suffering from whooping cough that the authors feel this method of infecting experimental animals may be most useful in the study of the disease. *F. T. Perkins*

De Bock, C. A. & Worst-Van Dam, A. M. **A Method for the Measurement of Antibodies against *Hemophilus pertussis* in Sera.** *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1960, v. 26, No. 1, 73–6.

Washed *Haemophilus pertussis* organisms were precipitated with ethanol, treated with 0·5% formalin, stained with hematoxylin and resuspended to give a final concentration of 5 x 10^{10} cells per ml. This suspension of coloured organisms was found to be stable when held at +4°C. for as long as 8 months and proved most useful as antigen in an agglutination test for pertussis antibody carried out in the cups of porcelain tiles.

Two drops of the antigen were mixed with equal volumes of serial serum dilutions and incubated at 37°C. for two hours, followed by 18 hours at room temperature at which time the patterns of agglutination were read.

The agglutination titres of control sera were similar with the use of this antigen to those obtained with fresh living suspensions of organisms. Similar results were also obtained with both antigens in agglutinin adsorption tests. *F. T. Perkins*

Andreesco, Viorica, & Vainer, Henriette. Recherches biologiques, chimiques et immuno-chimiques sur le sérum anti-pertussis. Note I. Préparation du sérum anti-pertussis de chèvre. [**A Chemical, Immunochemical, and Biological Study of Anti-Pertussis Goat Serum. 1st Note. Preparation of Anti-Pertussis Serum in Goats**] *Arch. Roumaines Path. Expér. et Microbiol.* 1960, Mar., v. 19, No. 1, 19–28, 4 figs. [33 refs.]

The English summary appended to the paper is as follows:—

"The methods used for the preparation of mixed anti-pertussis immune serum in goats and its biological properties are described. The antigens used for immunization were: living germs of *B. pertussis* in phase 1, endotoxin of the Besredka type, and antigens readily diffusing into physiologic saline. The details concerning the schedule of immunization are reported.

"From immune and from normal sera gamma-globulins and albumins were isolated by Kekwick's method (with SO_4Na_2) and by salting out with $SO_4(NH_4)_2$, respectively. Albumins, alpha-, beta-, and gamma-globulins were also isolated electrophoretically (details of the techniques are reported in note 2).

"In whole immune and normal serum as well as in all the fractions isolated, agglutinin titrations were carried out and the neutralizing and protecting actions were quantitatively determined.

"The results obtained show that in immune sera agglutinin titres range from 1/25,800 to 1/51,200 while gamma-globulins display a titre of 1/120,000. The neutralizing action amounted to 74–76% and the protecting action to 76–80%.

"Normal serum, normal alpha-, beta-, and gamma-globulins, normal albumin, as well as the alpha- and beta-globulins, and the albumin from immune sera do not contain agglutinins, and exert no protecting action. Albumin from immune sera displayed a low neutralizing power.

"The antigens used for immunization were likewise analysed by chemical and chromatographical methods. The two antigens were found to differ by their contents of reducing substances, the amount of which is 6 times higher in the antigen extracted with physiological saline.

"Diffusion tests in gels were performed with immune and normal sera and with the gamma-globulins isolated from them. Besredka's endotoxin and the readily diffusible antigen as well as whole germs were used as antigens. The results obtained show that whole serum as well as gamma-globulin react with the 3 antigens; the number of precipitation lines differs in each case.

"An immuno-electrophoretical investigation of the above mentioned fractions showed that antibodies against the whole germ and against the readily diffusible antigen were contained in the gamma-globulins, while those against the endotoxin were contained in gamma- and beta-globulins.

"On the whole, the data obtained demonstrate the utility of preparing mixed immune sera according to the above-described methods."

Vainer, Henriette & Andreesco, Viorica. Étude chimique, immuno-chimique et biologique du sérum anti-pertussis de chèvre. Note II. Préparation de la gamma-globuline anti-coquelucheuse. [**A Chemical, Immunochemical, and Biological Study of Anti-Pertussis Goat Serum. 2nd Note. Preparation of Anti-Pertussis Gamma-Globulin**] *Arch. Roumaines Path. Expér. et Microbiol.* 1960, Mar., v. 19, No. 1, 29–42, 7 figs. & 3 diagrams. [28 refs.]

Note. III. L'analyse par diffusion et immuno-électrophorèse en gel des sérums normaux et anti-pertussis de chèvre, des gamma-globulines et des albumines isolées de ces sérums. [**3rd Note. An Analysis of Normal and of Immune Goat Sera as well as of the Gamma-Globulins and Albumins isolated from them by Diffusion and Immuno-electrophoresis in Gels**] *Ibid.*, 43–58, 13 figs. [28 refs.]

The English summaries appended to the papers are as follows:—

Note II

"The methods used for the isolation of serum fractions from normal and from anti-pertussis sera are detailed. Sodium sulphate, ammonium sulphate, dialysis in the cold, and electrophoresis were used for this purpose.

"The products obtained, *i.e.* the supernatants as well as the precipitates, were analysed by electrophoresis at the end of each step of the procedure.

"As regards the possibilities of applying various methods of purification in practice for the preparation of anti-pertussis gamma-globulins, an analysis of the findings results in the conclusion that salting out with SO_4Na_2 appears to be the most adequate procedure. The product obtained is biologically active, non-pyrogenic, and contains 90% gamma-globulin, thus displaying a certain electrophoretic similarity to fraction II obtained by alcohol fractionation in the cold according to Cohn's method.

"Few data have been published concerning normal goat serum. This has determined us to investigate such sera by electrophoresis at various ages and to compare them with human sera and sera of laboratory animals. Gamma-globulins were found to be totally absent in the sera of new-born kids. Three to five days after birth they are present in rather considerable amounts. In the sera of normal adult goats the common serum fractions were found to exist. They display some peculiarities as regards electrophoretic mobility and the high contents of gamma-globulins are remarkable."

Note III

"Within the framework of a study concerning the physical and immunochemical properties of the whole sera and of the purified and concentrated serum fractions obtained from them, the respective reagents were analysed by the method of double diffusion in gels and by immunoelectrophoresis.

"The following antigens were used:

"Normal goat serum, normal gamma-globulin, normal albumin, anti-pertussis goat serum, anti-pertussis gamma-globulin, albumin from anti-pertussis serum.

"Antisera were prepared in rabibts by means of these antigens (at the point of maximal precipitation, the supernatants being tested for the presence of antigen or antibody).

"The following reagents were thus obtained:

"Serum against normal goat serum, serum against normal globulin, serum against normal albumin, serum against immune goat serum, serum against immune globulin, serum against immune albumin, serum against normal goat serum, adsorbed with normal goat serum, serum against normal globulin, adsorbed with normal globulin, serum against normal albumin, adsorbed with normal albumin, serum against immune goat serum, adsorbed with immune goat serum, serum against immune globulin, adsorbed with immune globulin, serum against immune albumin, adsorbed with immune albumin.

"These 18 immunochemical reagents were used in precipitin reactions in gels and for immunoelectrophoresis, in homologous as well as in heterologous patterns.

"An analysis of the results obtained in various conditions (as detailed above) led to the following conclusions:

"Multiple, specific and non-specific lines of precipitation were found to appear in diffusion reactions in gels. By eliminating the non-specific precipitation lines on the basis of results obtained in reactions with adsorbed sera, it has been possible to demonstrate the existence of a specific and dominant precipitation line for each single antigen.

"Specific and non-specific precipitation lines could be demonstrated and distinguished by immunoelectrophoresis as well. Anti-albumin and anti-globulin antibodies in rabbit sera were found to be contained in the gamma-globulin fraction. Besides antimicrobial antibodies, mixed anti-pertussis goat serum and gamma-globulins isolated from it appear to contain antitoxic antibodies as well (of the diphtheria antitoxin type, T fraction).

"In subsequent papers further data concerning the structure and biochemical and immunochemical properties of anti-pertussis gamma-globulin will be reported."

SCHMIDT, B. & LENK, V. Der Nachweis von Salmonellen im Abwasser als möglicher Massstab für die Seuchenlage einer Bevölkerung. [*Salmonellae* **in Sewage as a possible Indicator of the Epidemiological Situation in a Population**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 178, No. 4, 459–83, 2 figs. [47 refs.]

During a period of over 3 years, samples of sewage were collected from various sampling points on a Berlin sewage treatment farm and examined intensively for salmonellae. The technical methods used included a combination of membrane filtration with tetrathionate enrichment and subculture to Wilson and Blair medium. The detailed findings are listed in parallel with the salmonellae isolated from human subjects during the same period.

Of a total of 66 samples, 60 yielded one or more salmonellae; in all, 211 strains belonging to 26 different serotypes were isolated during the entire period. As many as 8 different serotypes were recovered from a single sample of sewage. Much the commonest was *Salm. paratyphi B*, followed by Salm. Give and Salm. Java. Typhoid bacilli were isolated only 3 times; the authors ascribe this to their rapid death in sewage rather than to technical difficulties in isolating the typhoid bacillus. The frequency distribution of the different phage types of paratyphoid B bacilli isolated corresponded closely to the known frequency of carriers of the different types. The authors cite also for comparison the isolations of salmonellae from animals, fish meal and frozen egg during the period of their investigation.

B. Moore

KAUFFMANN, F., LÜDERITZ, O., STIERLIN, H. & WESTPHAL, O. Zur Immunchemie der O-Antigene von Enterobacteriaceae. I. Analyse der Zuckerbausteine von Salmonella-O-Antigenen. [**The Immunochemistry of Enterobacteriaceae. I. Analysis of the Sugar Components of the Salmonella-O-Antigen**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 178, No. 4, 442–58. [62 refs.]

A number of previously unknown sugars, chemically dideoxyhexoses, have been demonstrated in recent years

in the lipopolysaccharide complexes of the O antigens of salmonellae [STAUB *et al.*, this *Bulletin*, 1959, v. 34, 669]. In the present intensive investigation, the authors extracted the lipopolysaccharide components of salmonella strains from all the O groups in the Kauffmann-White table. By further hydrolysis the individual sugars present were separated and identified by paper chromatography.

Only some of the more important findings can be briefly summarized here. Salmonellae of the same O group always shared the same component sugars, but the parallelism between serotype and "chemotype" was not complete, as a number of serologically unrelated O groups were also chemically alike. The 3 group A cultures examined all contained glucosamine, heptose, galactose, glucose, mannose, rhamnose and paratose. The last sugar was not found in any other O group. The 5 group B serotypes examined also contained 7 sugars, including again a dideoxyhexose, abequose, which was also shared by O groups C_2 and C_3. The sugar tyvelose was found in all the group D strains examined and in no other O group.

The different O groups contained from 4–7 different sugars, but all of them contained glucosamine, heptose, galactose and glucose. The clinically and epidemiologically important O groups A, B, C_2, C_3 and D all contained 7 sugars, of which one was a characteristic dideoxyhexose, *viz.*, abequose, paratose or tyvelose in the different groups.

The 36 different O groups or subgroups investigated could be classified into 16 "chemotypes" according to the component sugars found in the strains examined.

B. Moore

LÜDERITZ, O., O'NEILL, G. & WESTPHAL, O. Zur Immunchemie der O-Antigene von Enterobacteriaceae. V. Die antigenfaktoren in isolierten *Salmonella*-O-Antigenen. [**Immunochemistry of O Antigens of Enterobacteriaceae. V. Antigen Factors Isolated *Salmonella* O Antigens**] *Biochem. Ztschr.* 1960, v. 333, No. 2, 136–47. [22 refs.]

The English summary appended to the paper is as follows:—

"The polysaccharide O antigens of many *Salmonella* serotypes frequently carry more than one immunological specificity. These serotypes are classified in the Kauffmann-White scheme and characterized by the combination of antigen factors, the so-called antigen formula.

"9 purified *Salmonella* O antigens (lipopolysaccharides) of *Salmonella* groups A, B, C_1, C_2, D_1 and E were precipitated by selectively absorbed or suitable cross-reacting antisera. The precipitates so obtained were quantitatively analyzed for antibody protein and rhamnose (if present). They were further analyzed qualitatively for the known sugar constituents of the lipopolysaccharide used.

"On the basis of these experiments the location of the antigen factors 1, 2, 4, 5, 6, 7, 9, 12 and 27 on the respective lipopolysaccharides was demonstrated.

"The sugar analyses of lipopolysaccharides *before and after* cross-precipitation gave always identical results, no matter what antigen factor was involved in the reaction. There was no indication for any heterogeneity of the O-antigenic (lipo)-polysaccharides used for the serological precipitations. According to earlier conclusions, the various antigen factors of the O antigen complex of a given serotype appear to be linked at one and the same polysaccharide molecule. It is reasonable therefore that the *Salmonella* species investigated produce only one single O-antigenic polysaccharide as a constituent of their cell wall."

TINELLI, R. & STAUB, A. M. Étude immunochimique sur les *Salmonella*. VII. Étude des produits de l'hydrolyse acide ménagée du polyoside extrait de *S. typhi*. 1re Partie: Analyse de l'antigène O:12 du tableau de Kauffmann-White. [**Immunochemical Study of the Salmonellae. VII. The Products of Acid Hydrolysis of the Polysaccharide from *Salmonella typhi*. 1. Analysis of the O:12 Antigen of the Kauffmann-White Scheme**] *Bull. Soc. Chimie Biol.* 1960, v. 42, Nos. 5/6, 583–99, 3 figs. [21 refs.] 2e Partie: Analyse de l'antigène O9 du tableau de Kauffmann-White. [**2. Analysis of the O9 Antigen**] *Ibid.*, 601–10, 1 fig. [10 refs.]

STANDFAST, A. F. B. **A Report on the Laboratory Assays carried out at the Lister Institute of Preventive Medicine on the Typhoid Vaccines used in the Field Study in Yugoslavia.** *Bull. World Health Organization.* Geneva. 1960, v. 23, No. 1, 37–45. [10 refs.]

The report on the laboratory tests undertaken in Washington on the vaccines used in the same field study by EDSALL *et al.*, has already been published [this *Bulletin*, 1960, v. 35, 189]. As compared with the results of the field trials carried out at Osijek the results of the laboratory assays of the Yugoslav typhoid vaccines used in the trials are disappointing. A comparison of the laboratory results themselves obtained in England, the U.S.A. and Yugoslavia is somewhat confusing but it must be appreciated that although the 3 laboratories were nominally carrying out the same tests, they differed in detail with regard to the actual techniques employed. In collaborative investigations of this nature it is essential that at least one of the methods of assay employed by the participants should be identical in every detail. Nevertheless, apart from the greater H-agglutinogenicity of the phenolized vaccine—which has never been regarded as having protective importance—there was little or no laboratory evidence, from the active or passive mouse protection tests, of any difference in the potency of the two Yugoslav vaccines, yet the field tests in man showed significant differences. It can only be concluded from the results obtained that the mouse is not a suitable animal for the assay of typhoid vaccines or that a satisfactory method of using this animal for such assays has yet to be developed.

H. J. Bensted

STANDFAST, A. F. B. **Experiments with VI-Negative Strains of** *Salmonella typhi*. *Bull. World Health Organization*. Geneva. 1960, v. 23, No. 1, 47–52. [14 refs.]

[Before the typhoid Vi antigen was identified [FELIX and PITT, this *Bulletin*, 1934, v. 9, 562] the active protection test devised by PERRY, *et al.* [*ibid.*, 1934, v. 9, 771] showed that the protective potency of a typhoid vaccine against a subsequent challenge with a virulent organism was directly related to the mouse virulence, as measured by the MLD, of the culture used for the preparation of the vaccine. Although the technique of this original test was rather crude the results obtained were fairly consistent. For example, vaccines prepared from cultures whose MLD for mice were 500×10^6, 100×10^6 and 50×10^6 respectively protected mice against subsequent challenges of less than 1 MLD, 2 MLD and 6 MLD respectively. The high virulence organism had been derived from the very low virulence organism (the original classical Rawlings strain) in previous experiments with passage through mice. With the discovery of the Vi antigen it became possible to show that typhoid cultures containing a high complement of Vi antigen also had a high virulence for mice and since all the strains tested at that time which had a high mouse virulence were found to be rich in Vi antigen it was postulated that the mouse virulence was directly proportional to the Vi antigen content of the culture under test. Most freshly isolated strains of typhoid bacilli from the blood of patients suffering from typhoid fever contain Vi antigen although the amount in the first laboratory subculture may vary considerably. In a study of 450 freshly isolated cultures from the blood (BENSTED, *J. Roy. Army Med. Corps*, 1937, v. 68, 1; 1940, v. 74, 19) only 7% contained sufficient Vi antigen to be completely resistant to O antibody, but on the other hand less than 1% failed to show any evidence whatever of Vi antigen and the MLD of these strains was recorded as greater than 200×10^6 bacilli.

It must be appreciated that accurate determinations of Vi-content were not feasible except for a small proportion of the strains. The presence or absence of Vi antigen in the cultures was tested with a pure Vi serum with a culture of Ty. O 901 as a negative control which, in spite of the fact that KAUFFMANN [see this *Bulletin*, 1936, v. 11, 497] had shown it to contain Vi antigen after mouse passage, persistently failed to show any evidence of the antigen in the suspensions made from the laboratory stock strain.]

The present paper records some important and extremely interesting observations on a number of strains of *Salmonella typhi* classified as Vi-negative in accordance with their serological reactions and also in some cases by the very sensitive phage test. The author found to his surprise that several of these so-called Vi-negative strains, in the mouse virulence test, had a LD50 of less than 100×10^6 bacilli in saline suspensions without mucin. There seemed to be some explanation for this when he found that the organisms recovered from the mice from certain of the virulence tests were Vi-positive (these were examples of reversion of Vi-negative mutants from the classical Vi strain Ty 2), but 3 of the strains recently isolated for which the mouse LD50 respectively was 68×10^6, 82×10^6 and 119×10^6 bacilli showed no evidence of Vi antigen by the most sensitive tests even after 5 serial passages in mice. Moreover the survivors from sub-lethal doses of one of these strains when challenged 10 days later with more than 4 LD50 of the Vi-positive virulent Ty 2 strain were found to be almost fully protected. These completely unexpected results were fully investigated and the correctness of the original observations on both this strain, T 5501, and another were confirmed. In addition to the experiments outlined above it was found that if in the assessment of the potency of different typhoid vaccines by the active mouse protection test the protective effect of alcoholized as compared with phenolized vaccines was estimated with both the usual challenge of the Vi-positive strain Ty 2 and also the Vi-negative strain T 5501 the results could be very disturbing. In the field trials of the two types of vaccine, recently undertaken in Yugoslavia, the alcoholized vaccine, in which the Vi antigen should be preserved, was found to be less effective than the phenolized vaccine in which the Vi antigen was largely inactivated. The laboratory assessment by the author of the two vaccines using Ty 2 as the challenge showed little difference between the two, whereas with the Vi-negative strain T 5501 the phenolized vaccine appeared to be about 10 times more potent than the alcoholized.

[While there can be no question about the importance of Standfast's observations it is difficult to offer any satisfactory explanation. All the previous evidence had supported the thesis that the mouse virulence of typhoid bacilli was directly related to the Vi-content of the organism; in the light of the work reported here this must be modified, but how is not yet clear. It may well be that the factor responsible for mouse virulence and the development of mouse protective antibodies, which was previously thought to be an essential part of the Vi antigen, can on occasions be demonstrated separately from the Vi antigen. True Vi-negative strains of *Salm. typhi* are not commonly isolated from the blood of patients suffering from typhoid fever and all the strains encountered by the abstracter have had a mouse virulence of more than 200×10^6 bacilli as the LD50.

Further work is obviously indicated before the inviting characteristics of strain T 5501 could be accepted for the assessment of the potency of typhoid vaccines. Nevertheless this modest paper, in the face of all the difficulties of assessing the protective value of different typhoid vaccines, is most stimulating.] *H. J. Bensted*

COMBIESCO, Cornelia, CRĂCEA, E., GORUN, Eva & ELIAN, Inge. Étude des caractères biologiques des bacilles typhiques isolés des malades de fièvre typhoïde vaccinés et non-vaccinés au T.A.B. [**A Study of the Biological Characters of Typhoid Bacilli isolated from TAB-Vaccinated and Non-Vaccinated Typhoid Fever Patients**] *Arch. Roumaines Path. Expér. et Microbiol.* 1960, June, v. 19, No. 2, 267–81. [16 refs.]

The English summary appended to the paper is as follows:—

"Fourteen strains of typhoid bacilli isolated from typhoid fever patients who had not undergone TAB

vaccination and 8 strains of typhoid bacilli isolated from patients vaccinated with TAB at some time before the disease were investigated. The determinations concerned: the bacteriophage type, agglutinability by 'O' and 'Vi' sera, virulence, toxicity, aggressiveness, and immunogenicity. No relation was found to exist between the origin of the strains from one or the other of the two groups of patients and their various biological characters. An investigation of possible relations between the various biological properties of the same strains, irrespective of their origin (vaccinated or non-vaccinated subjects), showed a close relationship to exist between the virulence (invasiveness) and the immunogenicity of the strains. No close relationship is demonstrable between the antigenic structure and toxicity of the strains and their other biological characters.

"Testing of aggressiveness affords a useful method for the estimation of the pathogenicity of a typhoid strain. In most cases of protracted typhoid fever the strains isolated displayed a high degree of virulence and invasiveness."

BUCZOWSKI, Z. **A New *Salmonella* Type (S. Gdansk).** *Bull. Inst. Marine Med. Gdańsk.* 1960, v. 11, Nos. 1/2, 59–60.

"A new *Salmonella* type was described: *S. gdańsk*, serological formula *6, 7: l,v:* z_6."

VASSILIADIS, P., LE MINOR, L. & DONERS, J. Un nouveau sérotype de *Salmonella*: S. Ruki 1, 4, 5, 12: y: e, n, x. [**A New *Salmonella* Serotype: Salm. Ruki, 1, 4, 5, 12: y: e, n, x**] *Bull. Soc. Path. Exot.* 1960, Mar.–Apr., v. 53, No. 2, 134–5.

COLLARD, P. & SEN, R. **Salmonellae isolated at Ibadan. (Third Report: Strains isolated during 1958.)** *West African Med. J.* 1960, Aug., v. 9 (n.s.), No. 4, 172–4.

"Of the 29 species recorded for the first time in Nigeria, 13 were new, as follows:—

Salm. akanji	6, 8: r: 1, 7
„ *amina*	16: i: 1, 5
„ *aminatu*	3, 10: a: 1, 2
„ *apapa*	45: mt
„ *ayinde*	4, 12, 27: d: z_6
„ *garba*	6, 14, 25: a: 1, 5
„ *gege*	30: r: 1, 5
„ *jaja*	4, 12, 27: z_4, z_{23}
„ *kamoru*	4, 12, 27: y: z_6
„ *magumeri*	(1), 6, 14, 24, 25: eh: 1, 6
„ *molade*	(8), 20: z_{10}: z_6
„ *suberu*	3, 10: gm
„ *yaba*	3, 10: b: enz_{15}"

HOFMANN, P., HÖRCHNER, F. & WOLLE-JOHN, R. Einschleppung seltener Salmonellen durch importierte Geflügelfedern. [**The Introduction of Rare Species of *Salmonella* in Imported Fowl Feathers**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 178, No. 4, 484–91, 2 figs. [16 refs.]

Feathers and dust from a factory engaged in the processing of imported duck feathers for use in mattresses were examined for organisms of the *Salmonella* group. The feathers came mainly from China, Formosa and Korea, and to a lesser extent from other European countries and the United States. The feathers imported from the Far East were visibly contaminated with faecal matter and dust; those from Europe and America had been machine-plucked and washed with water. On arrival in the factory, all feathers were cleaned and heat-treated, but the dust removed from them was sold without further treatment for use in fertilizers or in the manufacture of pressed materials.

In all, 18 samples of feathers and 6 of dust were cultured for salmonellae. 7 samples of material from Europe or the United States yielded negative cultural results, but a wide range of salmonellae was isolated from samples from the Far East. By far the worst samples were from one batch of feathers imported from Hong-Kong. A sample of the feathers from this batch yielded *Salm. anatum*, Salm. Blockley, Salm. Derby, Salm. Kottbus, *Salm. meleagridis*, Salm. Newport and *Salm. typhimurium*; while dust from the same batch also yielded *Salm. bovis-morbificans*, Salm. Oranienburg, Salm. Potsdam and Salm. Senftenberg. No salmonellae were isolated from factory-processed feathers. *B. Moore*

VINCENT, J., NEEL, R. & LE MINOR, L. Les *Salmonella* des tortues. Contribution à l'étude des *Salmonella* du Maroc. [**Salmonella in Tortoises. Study of Salmonellae in Morocco**] *Arch. Inst. Pasteur de Tunis.* 1960, June, v. 37, No. 2, 187–94. [17 refs.]

The English summary appended to the paper is as follows:—

"An average of 78.5% of the continental tortoises from the region of Tangier (Morocco) harbor *Salmonella* in their body. This percentage is 96.3 for animals taken far from towns. Most of the animals harbor simultaneously several serotypes (up to 4). These *Salmonella* are localised in the terminal portion of the gut and in the rectum. We have found 15 different serotypes, one of which is new (*S. tangier*) and *S. virginia* having a phase 2 (1.2). Most of these serotypes have been described as agents of human infections."

[See also this *Bulletin*, 1956, v. 31, 1151, *bis*.]

MINTZER, Léonie. Étude de quelques souches de *S. cholerae suis* cultivées en présence de facteurs avec action antimicrobienne. [**A Study of some Strains of *S. cholerae suis* cultured in the Presence of Factors possessing an Antimicrobial Action**] *Arch. Roumaines Path. Expér. et Microbiol.* 1960, June, v. 19, No. 2, 295–301. [15 refs.]

HOBSON, D. **The Effect of Cortisone in Experimental Mouse Typhoid.** *Brit. J. Exper. Path.* 1960, June, v. 41, No. 3, 251–8, 2 figs. [21 refs.]

The experiments described here are a continuation of the author's previous work on *Salmonella typhi-murium* infection in mice [this *Bulletin*, 1956, v. 31, 804; 1958, v. 33, 65, 164 *bis*]. Employing the same methods of approach he studied the effects of cortisone on the mean death times, total bacterial population at time of death and the disturbance of the host-parasite equilibrium in the chronic carrier state, as seen in the survivors, and those recently infected in experimental infections with a virulent strain and two strains of lower virulence.

Cortisone was found to enhance the infectivity of *Salm. typhi-murium* for mice both for virulent strains and those strains of organisms of reduced virulence; the mean death times in days for untreated mice infected with the virulent strain was 11·2 whereas those treated with cortisone begun 5 days before infection had a mean death time of 2·4 days; with the less virulent strain the figures were 13·3 and 5·1 respectively. The final total bacterial population was not significantly different in any of the mice, treated or untreated, and whether the infection was with the virulent or the less virulent strains. It would appear that cortisone acts on the host factors so that the critical bacterial population determining death time is attained more quickly than in normal untreated animals. The full biological effect of cortisone in this respect is not observed unless treatment is commenced several days before infection. Cortisone did not upset the host-parasite equilibrium in mice where a chronic carrier state had been established. *H. J. Bensted*

KOVALEVA, N. I., YAKOVLEVA, A. V. & MIRONOVA, M. V. **Biological Properties of *Shigella sonnei* and *Shig. flexneri* grown in Synthetic Media under Conditions of Aeration.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 7, 77–82. [Translated from Russian.]

One serious disadvantage of growing organisms in bulk fluid (broth or synthetic) media under continuous aeration is the tendency of certain cultures to develop variants. The reviewer found many years ago (unpublished) that in spite of increased yields the method was not satisfactory for the preparation of standard agglutinable suspensions of Flexner bacilli owing to the increase in group antigens at the expense of the type specific antigens. Similarly with *Shigella sonnei*, Phase I—Phase II variation readily occurred even with the most carefully selected inoculum whereas it was possible to obtain from nutrient agar growths suspensions of *Sh. sonnei* of almost pure Phase I organisms. The longer growth was allowed to continue in the fluid medium the greater were the changes mentioned.

The authors of the present paper do not disclose the exact technique used but report that the biochemical characters of the Flexner and Sonne organisms tested did not change, neither did the virulence. There was some reduction in their agglutinability and the immunogenicity of vaccines prepared from the cultures varied according to the length of time they were allowed to grow. It was noted, however, that the mouse virulence of *Sh. sonnei* decreased significantly as the age of the culture increased, but loss of virulence of the same order was found with agar cultures of different ages. It is well known that the mouse virulence is almost entirely dependent on the proportion of Phase I and Phase II organisms in the culture; *Sh. sonnei* Phase II is practically avirulent for mice. *H. J. Bensted*

MORGUNOV, I. N., MAKSIMOVICH, N. A. & YAGUD, S. L. **The Search for an Experimental Model of Dysentery Infection—I. Reproduction of Dysentery Infection in Cats by Preliminary Sensitization.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 7, 24–31, 3 figs. [13 refs.] [Translated from Russian.]

The English version of this article is difficult to follow because the description of the experiments is somewhat confused. It appears, however, that the authors successfully reproduced dysenteric infections in cats by first injecting Shiga toxin subcutaneously and 24 hours later feeding the animals with cultures of *Shigella sonnei*. Typical intestinal lesions developed and the infecting organism could readily be isolated from the gut of the experimental animal. Similar results were obtained when the pre-infection treatment was a cuture filtrate of *Sh. sonnei* or killed bacterial cells of the same strain in place of Shiga toxin. When the authors speak of the toxin of *Sh. dysenteriae* it is presumed that they are speaking of a bacteria-free toxic filtrate of a culture of Shiga's bacillus, yet they several times state that *Sh. dysenteriae* could be isolated from the stools of the experimental animals throughout the experiments and it may well be that they used whole bacterial cultures of the living organism.

[It is of interest to note that the authors quote GRIGOR'EV (*Voenmed*, 1891, v. 171, 73) as having reproduced dysentery infections in kittens by infecting them *per rectum* after an ammonia enema. In the U.S.S.R. *Sh. dysenteriae* I is recognized as the Grigor'ev-Shiga bacillus and the implication of this reference is that Grigor'ev had already differentiated amoebic from bacillary dysentery and had identified the cause of bacillary dysentery some 7 years before Shiga's pronouncement (*Zent. f. Bakt. I, Abt., Orig.*, 1898, v. 23, 599). It will be recalled that another Russian worker, LOSCH (*Arch. Path. Anat. u. Physiol.*, 1875, v. 65, 196) described experiments in which he inoculated dysenteric exudates containing amoebae into dogs, by the rectal route, and reproduced a dysenteric condition in these animals. Whether the infection set up was a true amoebic dysentery or a mixed amoebic and bacillary infection is not known, but many years passed before the two diseases were shown to be separate entities. This was largely due to the painstaking studies of COUNCILMAN and LAFLEUR (*Johns Hopkins Hosp. Reports*, 1891, v. 2, 395) and KRUSE and PASQUALE *Ztschr. f. Hyg. u. Infektionskr.*, 1894 v. 16, 1) in which the distinctive pathological pictures of the two diseases were once and for all clearly differentiated. The details of Grigor'ev's experiments are not given by the authors of the present paper, neither are they available to the reviewer, but in considering any priority

claims for identification of *Sh. dysenteriae* it must not be forgotten that CHANTEMESSE and WIDAL (*Bull. Acad. Nat. Med.*, 1888, v. 19, 522) isolated an organism which they considered to be the cause of epidemic dysentery and which was subsequently shown by VAILLARD and DOPTER (*Ann. Inst. Pasteur*, 1903, v. 17, 463) to be identical to Shiga's bacillus.] *H. J. Bensted*

PETTENKOFER, H. J., MAASSEN, W. & BICKERICH, R. Antigengemeinschaften zwischen menschlichen Blutgruppen und Enterobacteriaceen. [**Antigenic Relationships between the Human Blood Groups and the Enterobacteriaceae**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1960, May, v. 119, No. 5, 415–29. [23 refs.]

That *Escherichia coli* O86:B7 contains an antigen similar to human blood group B substance has been shown by a number of workers [MUSCHEL and OSAWA, this *Bulletin*, 1960, v. 35, 192]. In the present study, a series of 30 rabbits were immunized with suspensions of *E. coli* O 86 grown in Sauton's medium. The antibody response depended on the blood group of the inoculated animals. Of 20 anti-A rabbits, *i.e.*, animals with a natural serum antibody reacting with human group A cells, 5 died in acute shock after the first injection, apparently because of a reaction between the organisms and the anti-A antibodies in the animals' sera. The survivors produced high levels of both anti-A and anti-B antibodies. The 10 group A rabbits, on the other hand, gave a very poor anti-B response, to titres of only 1:8 to 1:32. Neither series produced Forssman antibodies.

E. coli O 86 absorbed A and B antibodies from human group O sera, and the anti-A and anti-B agglutinins from group B and group A sera respectively. Similarly, the anti-A and anti-B antibodies produced in rabbits by immunization with *E. coli* O 86 were absorbed out by the appropriate human red cells and by the saliva of secretors.

No evidence of similar antigens was found in a parallel study of *Lactobacillus bifidus*. The authors agree with the suggestion of Wiener that antibodies to the blood group substances are formed in infancy in response to contact with coliform organisms and are not natural antibodies. *B. Moore*

BRINTON, C. C., Jr. & BARON, L. S. **Transfer of Piliation from *Escherichia coli* to *Salmonella typhosa* by Genetic Recombination.** *Biochim. et Biophys. Acta.* 1960, Aug. 12, v. 42, No. 2, 298–311, 2 figs. [16 refs.]

SAKAZAKI, R., NAMIOKA, S., NAKAYA, R. & FUKUMI, H. **Studies on So-Called Paracolon C27 (Ferguson).** *Japanese J. Med. Sci. & Biol.* 1959, Oct., v. 12, No. 5, 355–63, 2 figs. [11 refs.]

[There would seem to be little doubt that the *Bacillus pseudo-dysenteriae*, Type E, of KRUSE (*Ztschr. f. Hyg. u. Infektionskr.*, 1907, v. 57, 417) was the same organism as that described by SONNE (*Giftfattige Dysenteribacciller*, 1914, Copenhagen, Diss) and now known as *Shigella sonnei*. It is probable that the dysentery organism reported by DUVAL (*J. Amer. Med. Ass.*, 1904, v. 43, 381) was also identical but this is not so certain. Kruse was a very accurate observer and in view of the great controversy that had arisen some years previously when he had clearly demonstrated that Shiga's bacillus was non-motile, it is most unlikely that he would have given an incorrect description of his pseudodysentery bacillus, Type E. There was, however, some confusion about the question of the motility of Sonne's bacillus in the early 1920s, which is still fresh in the reviewer's mind although little was published, as far as can be remembered. At that time laboratories were beginning to report the isolation of Sonne's bacillus and its differentiation from Flexner was based on the delayed fermentation of lactose and agglutination by an anti-Sonne serum, which was considered conclusive. All the strains I isolated in Egypt [PERRY and BENSTED, *Trop. Dis. Bull.*, 1928, v. 25, 624] were non-motile, but colleagues occasionally reported motile forms; these were not further investigated. Some years later, however, FERGUSON and HENDERSON [this *Bulletin*, 1948, v. 23, 355] described a strain of *Escherichia coli*-C27—a slow lactose-fermenting motile organism—which possessed the major antigens of Phase 1 *Sh. sonnei* and EWING (*J. Bacteriology*, 1953, v. 66, 333) recorded the presence in the same stool of both typical *Sh. sonnei* and *Escherichia coli* C27.]

The present paper is concerned with a detailed examination of 22 strains of C27, including the original strain described by Dr. Ferguson. All the 22 strains possessed lophotrichous flagella and had identical biochemical characters. Serological studies showed that there were 5 different O antigen patterns and 4 flagellar patterns. Only one of the O antigen patterns was identical with that of *Sh. sonnei*; the others appeared to be unrelated. The 22 strains with the biochemical and morphological characters of C27 clearly form a group, of which those possessing the O antigens of *Sh. sonnei* are only a part. The authors consider that C27 should be classified as a *Pseudomonas* and propose the name *Ps. michigani* (the original strain was isolated in Michigan).

H. J. Bensted

ENGELBERG, Hanna & ARTMAN, M. **Absence of Carbon Monoxide-Sensitive Respiration in a Streptomycin-Dependent Mutant of *Escherichia coli* grown in Limited Amount of Streptomycin.** [Correspondence.] *Nature.* 1960, Aug. 27, v. 187, 801–2, 1 fig.

LITTAUER, U. Z., DANON, D. & MARIKOVSKY, Y. **Ribonucleic Acid from *Escherichia coli*: Electron Microscopical Study.** *Biochim. et Biophys. Acta.* 1960, Aug. 26, v. 42, No. 3, 435–41, 7 figs.

HEIFFER, M. H., MUNDY, R. L. & MEHLMAN, B. **Effect of Lethal Doses of Bacterial Endotoxin (*E. coli*) on Sympathetic Neurohormones in the Rabbit.** *Amer. J. Physiol.* 1960, June, v. 198, No. 6, 1307–11, 2 figs. [12 refs.]

PAPAZIAN, Ecaterina & MESROBEANU, Lydia. Recherches sur l'antigène Vi d'origine colibacillaire. [**Investigations concerning the Vi Antigen of Colibacillary Origin**] *Arch. Roumaines Path. Expér. et Microbiol.* 1960, June, v. 19, No. 2, 254–65.

GRÖNROOS, P. **Occurrence of *Bacterium anitratum* in Patients in a Central Hospital in Finland.** *Ann. Med. Exper. et Biol. Fenniae.* Helsinki. 1960, v. 38, No. 1, 1–8. [17 refs.]

Bacterium antitratum was isolated from 61 specimens of pathological material and from 1 sample of well water sent to a hospital bacteriological laboratory in Finland. 25 strains came from ears and 15 from urine. In 19 cases the specimens also yielded *Staph. aureus*, and in only 10 cases was *Bact. anitratum* the only organism present. The organism did not appear to have any great degree of virulence and the lesions from which it was isolated were mostly chronic or in patients with lowered general resistance.

[See also this *Bulletin*, 1958, v. 33, 690.]

R. E. O. Williams

VAN DRIMMELEN, G. C. **"Species" of *Brucella* Characterized by Phage Lysis.** *Bull. World Health Organization.* Geneva. 1960, v. 23, No. 1, 127–30.

The paper reports a further study of the Russian *Brucella* phage which previous workers [PARNAS *et al.* this *Bulletin*, 1958, v. 33, 1180; 1959, v. 34, 392] had found to be active against *Br. abortus* but not lysing strains of *Br. melitensis* or *Br. suis*. In the course of his studies the present author found a strain of *Brucella* of bovine origin which was resistant to the phage at a dilution of 10^{-2} but yielded a single plaque after treatment with the phage diluted 10^{-3}. On propagation on *Br. abortus* S 19 or Weybridge 544, this phage was found to lyse the standard *Br. suis* strain Minnesota 1330, but not *Br. melitensis* strains. The particular strain, on the culture of which the single plaque had developed, was fully examined by serological, cultural and biochemical, including dye sensitivity, tests and found to possess the characteristics of *Br. suis*. More extensive studies are obviously indicated but it would seem that the observations recorded in this paper, although of a preliminary nature, are highly suggestive. *H. J. Bensted*

JONES, Lois M. **Comparison of Phage Typing with Standard Methods of Species Differentiation in Brucellae.** *Bull. World Health Organization.* Geneva. 1960, v. 23, No. 1, 130–33. [Refs. in Footnotes.]

There have been several reports on the use of brucellaphage for typing strains of *Brucella* [PARNAS *et al.*, this *Bulletin*, 1958, v. 33, 1180; 1959, v. 34, 392], DIMITRIU *et al.*, *Ibid.*, 1960, v. 35, 929]. In all cases the phage used appears to have been derived from the Russian *Brucella abortus* phage, sometimes known as the "Tbilisi" phage. Typical strains of *Br. abortus* are consistently sensitive to this phage, but the results obtained with other brucellae seem to be less regular.

The present report in the main is in agreement with the previous findings. 31/38 strains of *Brucella* isolated from cattle and human beings were lysed by the phage. Most of these strains were typical *Br. abortus*, but some had the antigenic characters of *Br. melitensis* but had been isolated from cattle and the dye-reactions were not typical of *Br. melitensis*. Strains from Malta which included *Br. melitensis* and *melitensis*-like cultures isolated from goats, sheep, human beings and cattle and *Br. suis* strains were not lysed by the brucellaphage employed in the present study. *H. J. Bensted*

REDFEARN, M. S. & BERMAN, D. T. **Application of the Gel-Diffusion Technique for Typing Brucellae.** *Bull. World Health Organization.* Geneva. 1960, v. 23, No. 1, 133–4, 2 figs.

This paper presents further evidence [see BRUCE and JONES, this *Bulletin*, 1958, v. 33, 1180] that a diffusible precipitinogen which was readily obtained from smooth cultures of *Brucella melitensis* could not be demonstrated with similar preparations from *Br. abortus* or *Br. suis*. The present authors show that only cultures which were agglutinated by an absorbed monospecific *Br. melitensis* serum, irrespective of their other characteristics, produced a diffusible antigen. Cultures agglutinated by an absorbed monospecific *Br. abortus* serum showed no evidence of diffusible antigen. *H. J. Bensted*

TOMASZUNAS, S. **Comparison of the Properties of Virulent Strains and Attenuated Strains *B. tularense*.** *Bull. Inst. Marine Med. Gdańsk.* 1960, v. 11, Nos. 1/2, 47–51.

"None of the laboratory tests described, viz. examination of the morphology of cells and bacterial colonies, haemolysin production, requirement of cystine in the medium, agglutination reactions in acriflavine and physiological saline solutions as well as specific serum—could serve as tests determining for sure the biological properties of *B. tularense* populations, and did not allow distinction of the virulent from avirulent strains obtained due to attenuation.

"It seems that the biological test—infecting sensitive laboratory animals—is still the only sure test for determination of the virulence of *B. tularense* strains."

SUIRE, Andrée. Les vaccinations anti-*Brucella* par la souche vivante B. 112. Étude et comparaison de différentes méthodes sur souris. [**Anti-*Brucella* Immunization by means of the Living B. 112 Strain. A Comparative Study of Different Methods in Mice**] *Ann. Inst. Pasteur.* 1960, Aug., v. 99, No. 2, 241–52, 1 fig.

The English summary appended to the paper is as follows:—

"Different methods of immunization are successively studied:

"1. B. 112 strain alone.

"2. B. 112 associated with *melitensis* extracts (somatic and cell-wall constituents).

"3. B. 112 + an inert adjuvant.

"4. A toxoid of *B. melitensis*, alone or + B. 112.

"The mice receive only one immunizing injection and are challenged a month later with a highly pathogenic strain of *B. melitensis*. Necropsies are carried out from the seventh to the forty-ninth day. The best results are obtained with B. 112 + cell-walls of *B. melitensis*.

"These findings should be checked on other animal species."

BARTLEY, Eileen O. *Pasteurella septica* **in Chronic Nasal Sinusitis.** *Lancet.* 1960, Sept. 10, 581–2.

"A strain of *Past. septica* was isolated from a patient with frontal sinusitis in 1945 and again in 1959.

"Direct comparison of the two strains has not been possible, but they appear to be essentially similar except in certain biochemical properties and in penicillin sensitivity.

"Assuming that reinfection did not occur, *Past. septica* sinusitis may apparently be very chronic and last for as long as fifteen years."

[See this *Bulletin*, 1947, v. 22, 591.]

PITAL, A. **Growth Stimulation of** *Pasteurella pestis* **by a Combination of Coconut Water and Albumin Complex.** *J. Bacteriology.* 1960, June, v. 79, No. 6, 905–6.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 1261.]

GIESBRECHT, P. Über "organisierte" Mitochondrien und andere Feinstrukturen von *Bacillus megaterium.* [**On "Organized" Mitochondria and other Fine Structures in** *Bacillus megaterium*] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 179, No. 4, 538–81, 62 figs. (61 on 11 pls.) [Numerous refs.]

RAYNAUD, M., TURPIN, A. & BIZZINI, B., with the technical collaboration of L. SAGAERT. Existence de la toxine tétanique sous plusieurs états d'agrégation. [**Existence of Tetanus Toxin under Various Aggregation States**] *Ann. Inst. Pasteur.* 1960, Aug., v. 99, No. 2, 167–72, 1 pl. [11 refs.]

The English summary appended to the paper is as follows:—

"Pure tetanus toxin, with a titer of 3,300 Lf/mg N and 60 to 100 × 10^6 MLD/mg N (for mice) obtained by means of extraction of microbial cells, has a sedimentation constant of about 7 U.S. By action of cystein, then monoiodacetate, it can be depolymerized and yields a toxin which is still active and possesses a sedimentation constant of 4.5 U.S. By direct action of KCN, it is possible to obtain a substance possessing a S of 2.3.

"Tetanus toxin can therefore exist under various aggregation states. Depolymerization of the most aggregate forms can be carried out by rupture of disulfur bridges."

WARTENBERG, Janina. Rola acetylocholiny w zatruciu toksyną tężca. [**The Role of Acetylcholine in Poisoning with Tetanus Toxin**] *Archiwum Immunol. i Terapii Dośw.* Warsaw. 1960, v. 8, No. 2, 269–96. [40 refs.] English summary.

AIKAT, B. K. & DIBLE, J. H. **The Local and General Effects of Cultures and Culture-Filtrates of** *Clostridium oedematiens*, *Cl. septicum*, *Cl. sporogenes* **and** *Cl. histolyticum.* *J. Path. & Bact.* 1960, Apr., v. 79, No. 2, 227–41, 12 figs. on 3 pls. [15 refs.]

An earlier study of the lesions produced experimentally by *Cl. welchii* infection [this *Bulletin*, 1957, v. 32, 378] has been followed up by investigation of the pathological features of infections produced by *Cl. oedematiens* (*Novyi*), *Cl. septicum* (*Vibrion septique*) and *Cl. sporogenes* and *Cl. histolyticum.*

A good deal of this falls into line with the already established observations about these micro-organisms.

Points which are particularly emphasized are the similarity of the myo-necrotic lesion however it is initiated; the presence of a tissue-pervading element, hyaluronidase, in *Cl. septicum* infections and the observation that although it rarely, if ever, appears in human lesions except as a mixed infection, *Cl. histolyticum* is capable of developing increased pathogenicity for the rabbit as a result of repeated passage. Another point of considerable interest was that the *Cl. histolyticum*, so intensely destructive of muscle *in vivo*, was not as active as *Cl. sporogenes* in disintegrating dead muscle *in vitro.*

In the muscle lesion due to *Cl. histolyticum* the argyrophil reticulum disappears owing to the action of a collagenase or allied ferment. This does not occur in the muscle lesions due to *Cl. oedematiens.*

J. W. McLeod

LABOUESSE, B.; GROS, P. La clostripaïne, protéase de *Clostridium histolyticum.* I. Purification et activation par les thiols [LABOUESSE & GROS]. [**Clostripain, a Protease of** *Clostridium histolyticum.* **I. Purification and Activation by Thiols.** *Bull. Soc. Chimie Biol.* 1960, v. 42, Nos. 5/6, 543–58, 6 figs. [20 refs.] II. Spécificité [GROS & LABOUESSE]. [**II. Specificity**] *Ibid.*, 559–68, 2 figs. [15 refs.]

HEINRICH, S. & PULVERER, G. Über den Nachweis des Bacteroides melaninogenicus in Krankheitsprozessen bei Mensch und Tier. [**Isolation of** *Bacteroides melaninogenicus* **in Human and Animal Disease**] *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 146, No. 4, 331–40. [22 refs.]

A large collection of strains of these anaerobic bacteria which produce black colonies on media containing

haemoglobin has been made. 621 strains were obtained from human and a few more from animal lesions.

The strains were obtained in most instances from lesions about the face, neck and mouth, but a considerable number from pulmonary lesions or from suppurations associated with the urinary, intestinal and genital tracts.

These micro-organisms are mostly found in cases of mixed infections, and are commonly associated with other anaerobes or with peroxide-forming streptococci. The fact that in 4 cases they were the only bacteria grown from a lesion and that in several others the only other element in the mixed culture was a coagulase negative staphylococcus appears to the authors to be adequate evidence that the *Bacteroides melaninogenicus* is a genuinely pathogenic form.

There is no convincing evidence of a special pathogenic association with any other bacterial species.

J. W. McLeod

PULVERER, G. & HEINRICH, S. Infektionsversuche an Laboratoriumstieren und *in vitro*-Untersuchungen zur Fermentausstattung des *Bacteroides melaninogenicus*. [**Investigation of the Infection of Experimental Animals and the Production of Ferments by** *Bacteroides melaninogenicus*] *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 146, No. 4, 341–9. [16 refs.]

51 strains from various sources, human and animal, were tested for pathogenicity in rabbits, mice and guinea-pigs. The mouse proved refractory but in a small number of instances a process of necrosis and gangrene with pyaemic developments was produced in the rabbit or guineapig.

Coagulase is produced but it is more often active on rabbit than on human plasma. On the other hand the fibrinolysin which they produce attacks fibrin from human plasma most actively. Ferments of the nature of hyaluronidase were not recognized. *J. W. McLeod*

WEBER, M. M. **Factors influencing the *in vitro* Survival of *Treponema pallidum*.** *Amer. J. Hyg.* 1960, May, v. 71, No. 3, 401–17, 4 figs. [36 refs.]

This article is highly technical and as such should be studied in the original by those who propose to try to culture virulent *Treponema pallidum in vitro*.

It may be said at once that this author was unable to keep these organisms alive for more than about 16 days so that the problem has not yet been solved.

A medium is described which contains no less than 29 different ingredients; the most important of these appear to be pyruvate, sodium chloride and a sulphydryl compound; for prolonged survival acid hydrolysed gelatin, albumin, ultrafiltrate or ox serum and inorganic phosphates are necessary.

One considerable advance in technique was that anaerobic jars are not necessary and an "oil-barrier" is just as effective; this saves a great deal of labour. Under the best conditions organisms usually died after 8–12 days; this may be due to exhaustion of food supply and metabolites and the accumulation of toxic end-products, but renewal of the medium was not successful; another explanation is formation of residual antibody from the rabbits' testes.

The fact that spirochaetes grow most strongly in the rabbits' testes and in the human foetus suggests that the *in vivo* growth of spirochaetes is stimulated by actively growing tissue; the use of tissue-culture techniques is therefore envisaged. [What is remarkable is that it is easy to grow non-virulent (Reiter) spirochaetes but impossible to grow virulent ones though the two appear to have much in common.]

[See also this *Bulletin*, 1948, v. 23, 1002.]

T. E. Osmond

ADAMOV, A. K. **The Influence of Certain Organic Compounds on the Growth of Pathogenic Leptospires.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 8, 126–30, 2 figs. [Translated from Russian.]

From a review of some of the literature on the metabolism of pathogenic leptospires, a subject as yet inadequately studied, the author draws certain conclusions. It would seem that crude serum protein is not a basic nutritional requirement of leptospires; that carbohydrate metabolism has not been demonstrated; and that peptone, creatinine, cysteine, and a few vitamins (B1, PP [*sic*, ? nicotinic acid], and B2) stimulate growth of the organisms.

The author studied the influence of various substances on the growth of laboratory strains of *Leptospira icterohaemorrhagiae*, *L. grippotyphosa*, and *L. pomona*. Each test substance was added, in various concentrations, to 5 ml. of Sorensen's phosphate buffer (diluted 1 in 10) containing 0·5% inactivated rabbit serum. The inocula consisted of 0·5 ml. of 7-day cultures of leptospires grown in a medium containing 0·5% rabbit serum and incubated at 30°C. Progress was assessed by counting leptospires in 20 visual fields (using a 40×7 optical system) in preparations of 0·5 ml. of culture under coverslips of standard size: the mean count per field was the unit derived.

Growth of leptospires was stimulated by urea in a concentration of 100 μgm./ml., and in concentrations of 1–5 μgm./ml. of the following amino-acids: alanine, valine, glutamic acid, glycine, leucine, lysine, methionine, cysteine, histidine, tryptophan, tyrosine and β-phenylalanine. Creatinine was markedly stimulating and the maximum effect was given by a concentration of 1,000 μgm./ml. of medium. [A graph indicates that the field counts for test and control after 7 days' incubation were respectively 70 and 20, while after 20 days' incubation both were about 60.]

When carbohydrates were tested, growth continued with all when they were present in a concentration of 50 μgm./ml. and with some at 1,000 μgm./ml. while others had an inhibiting effect at 500 μgm./ml. or more. The inhibiting effect was attributed to the presence of aldehyde and ketone groups: thus glucose, fructose and galactose suppressed growth of leptospires at 500 μgm./ml., whereas the corresponding polyhydroxy alcohols did not. Xylose and arabinose, lactose and maltose were

likewise suppressive; but sucrose, raffinose, starch and inulin supported growth even at 1,000 μgm./ml.

Raffinose was particularly effective after the first few days of incubation. A graph indicates that the test and control counts of leptospires per visual field were as follows: at 3 days, about 15 for each; at 7 days, 70 and 26; at 16 days, 100 and 25.

Vitamin B1 stimulated the growth of all the leptospires; nicotinic acid stimulated only *L. pomona*. Four other vitamins (pyridoxine, riboflavine, folic acid, calcium pantothenate) did not influence the growth of leptospires when tested in concentrations of 1–10 μgm./ml., while higher concentrations were inhibitory.

No influence on growth was observed with uracil and choline in concentrations of 1–10 μgm./ml.

The author was unsuccessful in his attempts to prepare a serum-free synthetic medium for the culture of leptospires. *L. H. Turner*

Füzi, M. & Csóka, Rózsa. Die Differenzierung der pathogenen und saprophytischen Leptospiren mittels eines Kupfersulfattestes. [**Differentiation of Pathogenic and Saprophytic Leptospirae by means of a Copper Sulphate Test**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 179, No. 2, 231–7.

The divergencies in opinion about the validity of varying sensitivity to copper ions for distinguishing pathogenic from saprophytic leptospires, a test first introduced by Shiga in 1924, has led the authors to re-examine the question. They consider that the use of sources of copper ions, unlikely to be constant, is responsible for the divergencies in opinion and they have sought to standardize the test. A large selection from the known pathogenic forms, including several from each group, and also a collection of water leptospires from many different sources have been examined. Korthof's medium containing various dilutions of $CuSO_4$ was used.

With a 1/100,000, and a 1/1,000,000 concentration of $CuSO_4$ in Korthof's medium with 10% rabbit serum and added haemoglobin, it was found that all pathogenic strains grew in the second and in control tubes but not in the first. The water strains grew in all three tubes.

There were two exceptions, *Leptospira semaragana* and *L. andamani*, which grew in the first tube. These the authors consider from this and other evidence to have been mistakenly described as pathogenic forms.

J. W. McLeod

Ghosh, S. N. & Mukerjee, S. **Studies on Antigens of *Vibrio cholerae* by Gel Diffusion Technique. Part I: Observations on the Antigenic Make-up of Soluble *Vibrio* Materal.** *Ann. Biochem. & Exper. Med.* Calcutta. 1960, Feb., v. 20, No. 2, 31–6, 6 figs. [15 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 1263.]

Krishna Murti, C. R. **Action of Streptomycin on *Vibrio cholerae*.** *Biochem. J.* 1960, Aug., v. 76, No. 2, 362–9, 5 figs. [32 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 1263.]

Gallut, J., with the technical collaboration of J. Quiniou. Contribution à l'étude du complexe antigénique "O" des vibrions. Relations immunologiques entre *V. cholerae* et vibrions dits inagglutinables (NAG). [**Studies on the *Vibrio* Antigen "O" Complex. Immunological Relationships between *V. cholerae* and the so-called "Non-Agglutinable" Vibrios (NAG)**] *Ann. Inst. Pasteur.* 1960, July, v. 99, No. 1, 28–55, 3 figs. [24 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 1262.]

RICKETTSIAE

WEISS, E. & DRESSLER, H. R., with the technical assistance of I. E. FISHBURNE. **Selection of an Erythromycin-Resistant Strain of** *Rickettsia prowazekii*. *Amer. J. Hyg.* 1960, May, v. 71, No. 3, 292–8. [24 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 1155.]

IGNATOVITCH, V. F. **The Comparative Survival of** *Rickettsial prowazeki*, *R. mooseri* **and** *R. burneti* **during Vacuum Preservation.** (Author's summary.) *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 7, 150–51. [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 1155.]

SHISHIDO, A., OHTAWARA, M., HIKITA, M. & KITAOKA, M. **The Nature of Immunity against Scrub Typhus in Mice. II. The Cross-Protection Test with Mice for Identification and Differentiation of Several Strains of** *Rickettsia orientalis* **newly isolated in Japan.** *Japanese J. Med. Sci. & Biol.* 1959, Dec., v. 12, No. 6, 391–404, 4 figs. [Numerous refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 1256.]

LI BIN. **Cultivation of** *Dermacentroxenus sibiricus* **in Lice and the Preparation of a Corpuscular Antigen from Lice.** *J. Microbiol., Epidemiol., & Immunobiol.* London. 1959, v. 30, No. 8, 76–82, 5 figs. [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 1256.]

IGNATOVICH, V. F. **The Course of Inactivation of** *Rickettsia burneti* **in Fluid Media.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 9, 134–41. [14 refs.] [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 1257.]

BACTERIOPHAGES

WILSON, D. E. **The Effects of Ultraviolet Light and Ionizing Radiation on the Transduction of** *Escherichia coli* **by Phage P1.** *Virology*. New York. 1960, July, v. 11, No. 3, 533–46, 4 figs. [11 refs.]

When *Escherichia coli* was infected with P1 phage at high multiplicity and transduction of the markers governing threonine and leucine requirements occurred, the transduced cells were found to be lysogenic. UV induction of these lysogenic cells produced phage possessing a high efficiency of transduction, of up to 10^{-1} per plaque-forming particle in some cases.

8 lysogenic clones carrying phage with a high efficiency of transduction were studied. The rate at which UV-irradiation of the lysates destroyed the ability of the phage strains to transduce threonine or leucine markers, separately or both together, was found to be the same. However, 2 types of inactivation curve were observed, 1 strain being quite different from the rest. Gamma-irradiation of this one strain also gave inactivation results which were different from those of the other strains. The author remarks that the one strain must carry more DNA than the rest, as sensitivity to gamma-irradiation depends on DNA content. There is no information about the proportion of DNA which comes from the host. *Janice Taverne*

FAGUET, M. Effet inducteur de l'eau oxygénée sur la production de phage par la souche lysogène *Escherichia coli* K12.(λ). [**Inducing Effect of H_2O_2 on Phage Production by** *Escherichia coli* **K12** (λ)] *Ann. Inst. Pasteur.* 1960, Aug., v. 99, No. 2, 297–301, 4 figs.

The English summary appended to the paper is as follows:—

"The production of phage by the *E. coli* K12 (λ) strains used in the experiments is markedly increased in presence of H_2O_2 at a concentration of about M/2,000."

ROSENTHAL, H. A. & EDLIGNER, E. De l'influence du chloroforme sur le rendement d'*Escherichia coli* B en phages T-pairs. [**Influence of Chloroform on Burst Size of Even T Phages by** *E. coli* **B**] *Ann. Inst. Pasteur.* 1960, Aug., v. 99, No. 2, 302–5.

The English summary appended to the paper is as follows:—

"The addition of chloroform to lysates of mass cultures or to lysates of single bacteria infected with the even T phages is followed by an actual increase of the burst size of active phages.

"This increase does not seem to be due to an activation of phages which would be inhibited in a mass lysate. "This phenomenon is not observed with T1 and T5 phages. The possible mechanisms of this action are discussed."

BENDET, I. J., GOLDSTEIN, D. A. & LAUFFER, M. A. **Evidence for Internal Organization of Nucleic Acid in T_2 Bacteriophage.** [Correspondence.] *Nature.* 1960, Aug. 27, v. 187, 781–2, 2 figs.

LITMAN, Rose M. & PARDEE, A. B. **The Induction of Mutants of Bacteriophage T2 by 5-Bromouracil. III. Nutritional and Structural Evidence regarding Mutagenic Action.** *Biochim. et Biophys. Acta.* 1960, July 29, v. 42, No. 1, 117–30, 3 figs. [25 refs.] **IV. Kinetics of Bromouracil-Induced Mutagenesis.** *Ibid.*, 131–40, 6 figs. [24 refs.]

SHUG, A., MAHLER, H. R. & FRASER, D. **Studies in Partially Resolved Bacteriophage-Host Systems. VI. The Involvement of Ribonucleic Acid in Various Aspects of the Reproduction of Bacteriophage T2.** *Biochim. et Biophys. Acta.* 1960, Aug. 12, v. 42, No. 2, 255–71, 2 figs. [57 refs.]

CARO, L. G. & KAHN, Phyllis. **The Uptake of [^{3}H] uridine in Normal and Filamentous Forms of *Escherichia coli* infected with T-2 Bacteriophage.** *Biochim. et Biophys. Acta.* 1960, Aug. 12, v. 42, No. 2, 351–4, 3 figs.

VELAUDAPILLAI, T. **Phage Mediated Appearance of Somatic Antigen 5.** *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 146, No. 6, 548–51.

"Phage P22 grown on *Salm. chester* in addition to effecting lysogenic conversion of somatic antigen 1 and transduction was able to cause the appearance of somatic antigen 5 in non-embryonated eggs and embryos but not *in vitro*. The phages carried by the transduced strains were not able to produce somatic antigen 5."

CIUCĂ, M., MEITERT, T., MEITERT, Eugenia & MEITERT, S. Capacité "inductrice" de l'isotope radioactif cobalt 60 (Gamma Irradiation), avec production de phage lytique actif, des "écosystèmes phages-souches de *Pseudomonas aeruginosa* soumis à l'action de cet agent. **[The "Inducing" Capacity of the Radioactive Isotope Cobalt 60 (Gamma Rays). Production of Active Lytic Phage from "Oecosystems" of Phage—*Pseudomonas aeruginosa* Strains subjected to the Action of this Inducing Agent]** *Arch. Roumaines Path. Expér. et Microbiol.* 1960, June, v. 19, No. 2, 173–9. [11 refs.]

VIRUSES

The order in this section is:—**General; Psittacosis-Lymphogranuloma group; Pox group; Respiratory group; Reovirus group; Enteric group; Arthropod-borne group; Others.**

PATTYN, S. R., DELVILLE, J. P. & PEEL, J. Sensibilité comparée des cultures de cellules amniotiques humaines et des cultures de cellules HeLa, Monkey-Heart, Detroit-6 et L 929 vis-à-vis de divers virus. **[Comparative Sensitivity of Human Amnion and of HeLa, Monkey-heart, Detroit-6 and L929 Cell Cultures to Various Viruses]** *Ann. Soc. Belge de Méd. Trop.* 1960, Feb. 29, v. 40, No. 1, 215–23. [19 refs.]

The following cell culture systems were used: Hela, Detroit-6, monkey-heart, L929 strain mouse fibroblasts as continuous lines, trypsinized human amnion cells in primary culture. Polioviruses 1, 2 and 3 caused cytopathic changes (CP) in all except L929. Of ECHO viruses, only types 1–3 and 5–14 caused CP in only human amnion. Of Coxsackie B viruses, types 1 and 2 affected none of the cultures while types 3, 4 and 5 caused CP in all except L929. Coxsackie A viruses were tested only against Hela in which a number caused doubtful CP, and human amnion in which CP was caused by types 9, 11 (1 of 2 strains), 13 (1 of 2 strains), 15 (1 of 2 strains) and 18, but not by 6 or 14. The strains which gave no CP were highly pathogenic for suckling mice while those which did had lower mouse pathogenicity. Adenoviruses types 1–11 caused CP in all except L929 cells. Vaccinia and herpes viruses caused CP in all the cell cultures. Columbia SK (encephalomyocarditis) virus caused no CP in any. GD VII (mouse encephalomyelitis) virus caused no CP in either Hela or amnion cells. Western equine encephalitis, Semliki Forest, Sindbis, St. Louis encephalitis, Japanese encephalitis, Russian spring-summer encephalitis, dengue 1 and 2, yellow fever (17D), West Nile, Ntaya and Bwamba viruses gave no CP with any of the cell cultures. Eastern equine encephalitis and Bunyamwera viruses gave CP only with human amnion and L929 cells.

Details are given of the origin and passage levels of the strains used. *C. E. Gordon Smith*

PHILIPSON, L., ALBERTSSON, P. Å. & FRICK, G. **The Purification and Concentration of Viruses by Aqueous Polymer Phase Systems.** *Virology.* New York. 1960, July, v. 11, No. 3, 553–71, 3 figs. [21 refs.]

The distribution of a substance in a 2-phase system made up of 2 polymer solutions depends upon particle size as well as surface properties. Owing to their large size, virus particles tend to collect in 1 phase only, while other components of the virus suspension are distributed differently. If this phase has a smaller volume than the original virus suspension, then the virus will be concentrated as well as purified.

This paper describes the purification and concentration of T2 phage, ECHO, influenza and adenoviruses by using different phase systems made up of sodium dextran sulphate and polyethylene glycol, polyvinyl alcohol or methyl cellulose. Best results were obtained by repeated extractions, a concentration of about 1,000-fold being possible in 2 steps. Methods of eliminating the polymer from the virus-containing phase are given. Purified preparations were examined under the electron microscope and their UV absorption spectra were also analysed. The results indicated that the method would be most useful for the larger viruses. *Janice Taverne*

SUNAGA, H., TAYLOR, R. M. & HENDERSON, J. R. **Comparative Sensitivity of Viruses to Treatment with Diethyl Ether and Sodium Desoxycholate.** *Amer. J. Trop. Med. & Hyg.* 1960, July, v. 9, No. 4, 419–24, 1 fig. [13 refs.]

Equal volumes of virus suspension and diethyl ether were mixed and kept in the refrigerator for 24 hours. The ether was then removed by evaporation. Equal amounts of virus suspension and sodium desoxycholate (1:200 and 1:1,000) were mixed and incubated at 37°C. for 1 hour. The resultants and comparable controls were titrated in tissue culture or embryonated eggs.

6 enteroviruses were tested: poliovirus 2, Coxsackie A-9 and B-1, ECHO 1, 6, and 9. All were resistant to both ether and desoxycholate. All 3 adenoviruses (1, 2 and 3) tested were also resistant to both. Both influenza A and B were markedly reduced in titre by both desoxycholate (1 : 1,000) and ether although not completely inactivated by either.

10 arthropod-borne viruses were tested: 3 in group A, 3 in group B, 2 in group C, Bunyamwera and California. All were completely inactivated by both desoxycholate (1:1,000) and ether. Sodium desoxycholate was found to be toxic to chick embryo and hamster kidney cultures. 6 of the arthropod-borne viruses were tested against dilutions of desoxycholate from 1:500 to 1:4,000. West Nile was most sensitive being completely inactivated by 1:4,000; California and Bunyamwera by 1:2,000; Japanese encephalitis by 1:1,000; and eastern equine encephalitis and Sindbis viruses by 1:500.

C. E. Gordon Smith

TERZIN, A. L. **Different Types of Serologic Reactivity to Bedsonia (Psittacosis Group) Antigen in Various Hosts. Discussion of some Related Problems.** *J. Immunology.* 1960, July, v. 85, No. 1, 90–98, 1 fig. [15 refs.]

Antibodies produced by many avian and some mammalian species form complexes with homologous antigens which do not fix guineapig complement. This is true of certain viruses of which those of the ornithosis group are an example. Ornithosis antibodies which fail to give a direct complement-fixation test (CF) but are revealed by an indirect complement-fixation inhibition test (CFI) are described as incomplete. There is some evidence that the completeness of antibodies is not an absolute quality but a relative one dependent on the preparation of antigen used. Evidence is advanced which strongly suggests that the presence of so-called incomplete antibodies is responsible for prozones occurring in the direct test (CF).

Using the CF and the CFI the author has examined 447 sera containing ornithosis antibodies, from various mammalian and avian species; he has also examined artificial mixtures of sera containing known concentrations of either complete or incomplete antibody. 3 types of reaction were observed:

I CF+ but CFI−
II CF− but CFI+
III both tests giving positive reactions.

All horse sera, almost all human sera and the majority of cattle, sheep and pig sera gave a type I reaction. Those from duck, goose, hen or turkey were of type II. Almost without exception those mammalian sera not giving the direct test were of the type II category. The only examples of the type III reaction were provided by 20 out of 77 pigeon sera and 1 out of 76 sheep sera. In the type III reaction the direct reaction shows a prozone the height of which equals the titre of the CFI. Results obtained with varying mixtures of CF+ and CFI+ sera suggest that both types of antibody—complete and incomplete—compete for the antigen with the complete or partial suppression of their respective activities, resulting in CF+ alone, CFI+ alone or both CF+ and CFI+ with prozoning in the former. *S. P. Bedson*

GORDON, F. B.; BLOOM, H. H.; MAMAY, H. K.; TRIMMER, R. W. **Studies with Drug-Resistant Strains of Psittacosis Virus. I. Comparison of Four Strains used in Mixed Cultures** [GORDON, BLOOM & MAMAY]. *Virology.* New York. 1960, June, v. 11, No. 2, 474–85, 4 figs. **II. Derivation of Strains with Dual Drug Resistance from Mixed Culture of Singly Resistant Strains** [GORDON, MAMAY & TRIMMER]. *Ibid.,* 486–98, 3 figs.

I. In the first of these two papers the results of the re-examination in the chick embryo of 3 drug-resistant strains of psittacosis virus—sulphonamide-resistant, sulphonamide- and penicillin-resistant and chlortetracycline-resistant—are reported. Each form of drug resistance was manifested in a manner somewhat peculiar to itself. Resistance of the first 2 was largely independent of the dose of drug used, the sulphonamide-resistant strain killing embryos as promptly in the presence of sulphonamide

as in its absence, and the death of the embryos infected with the sulphonamide-penicillin-resistant strain was only delayed 1 or 2 days over a wide range of doses of penicillin. The resistance to chlortetracycline, however, was dependent on drug dose when the infecting dose of the resistant strain was small. These differences are thought to reflect differences in mode of action of these drugs and thus of the mechanism of resistance to them.

II. The second paper reports an attempt to produce a strain possessing dual drug resistance from 2 mono-resistant strains. Mixed infections of chick embryos with sulphonamide-resistant and chlortetracycline-resistant strains were screened in the presence of both these drugs simultaneously. Dual-drug-resistant variants were repeatedly obtained under conditions in which infection with these 2 strains, singly or in combination with the drug-sensitive strain from which the resistant ones were derived, did not give rise to dual-drug-resistant strains. The dual resistance of these new strains persisted after passage in the absence of drugs, high-dilution passage and passage in the presence of the drugs singly. The authors consider that the evidence suggests specific interaction between the 2 mono-resistant strains.

S. P. Bedson

Aderca, I. & Ianconescu, M. Cercetări asupra virusului herpetic în culturi de celule embrionare si amniotice umane. [**Investigations on Herpes Virus in Human Embryo and Amnion Cell Cultures**] *Microbiol., Parazitol., Epidemiol.* Bucharest. 1960, Mar.–Apr., v. 5, No. 2, 155–62, 4 figs. [12 refs.] English summary.

Primary explant cultures of human embryo fibroblasts were found to be suitable for the primary isolation of herpes virus, and 6 strains of virus could be isolated from vesicle fluid from 6 patients suffering from herpes simplex. Herpes virus was similarly isolated from the nasopharyngeal washings of 6 patients suffering from other diseases (non-diphtheritic croup, ulcerative stomatitis, pharyngitis and measles), and from the central nervous system, of a patient who had died of encephalomyelitis. A cytopathic effect appeared 24–96 hours after infection of the cultures, and the strains of virus obtained was identified in all cases by neutralization tests. The cytopathic effect produced by herpes virus in human embryo fibroblast and human amnion cell cultures is described and illustrated in photomicrographs. *D. J. Bauer*

Lépine, P., Artzet, F. & Ceolin, G. Conservation du virus herpétique. [**Preservation of Herpes Simplex Virus**] *Ann. Inst. Pasteur.* 1960, May, v. 98, No. 5, 750–53, 1 fig.

"By means of addition of skim milk to infectious material it is possible to preserve herpes simplex virus for at least six months. If the virus is diluted by half in milk, it can be freeze-dried, frozen, even kept at +4°C. without any important decrease of the infectious titre."

[The virus came from tissue cultures.]

Endo, M. *et al.* Étude du virus B au Japon. I. Recherche des anticorps neutralisant le virus B chez les singes d'origine Japonaise et les singes étrangers importés au Japon. [**Study of B Virus in Japan. I. Investigation of Neutralizing Antibodies in Japanese Monkeys and in Monkeys from other Countries Imported into Japan**] *Japanese J. Exper. Med.* 1960, June, v. 30, No. 3, 227–33, 4 figs. on pl. [17 refs.]

Traver, Myrna I., Northrop, R. L. & Walker, D. L. **Site of Intracellular Antigen Production by Myxoviruses.** *Proc. Soc. Exper. Biol. & Med.* 1960, June, v. 104, No. 2, 268–73, 1 fig. [15 refs.]

Influenza A (PR8), Newcastle disease virus (NDV), mumps virus and the Sendai strain of para-influenza 1 virus were grown in tissue cultures of chick embryo lung and human conjuctival cells (Chang). The cells were stained with antisera prepared by infecting laboratory animals and conjugated with fluorescein. All sera used were shown to have high levels of antibody against the V and S antigens of the appropriate virus. The growth of the virus in the cultures was measured by haemagglutination and infectivity titrations, in order to determine whether incomplete or fully infectious virus was being formed. Cells infected with influenza virus showed staining first in the nucleus and later in the cytoplasm. Cells infected with Sendai, NDV and mumps virus showed staining only in the cytoplasm, although efforts were made to ensure that complete infectious virus was being formed. The authors point out that others have obtained similar results to theirs; they suggest that the formation of stainable antigen in the nucleus may be a feature distinguishing the influenza virus group from other myxoviruses.

[It will be necessary to use specific anti-V or anti-S antisera to determine which antigens of mumps, NDV and Sendai viruses are being stained, and possibly whether the S antigen in these viruses is found only in the cytoplasm instead of in the nucleus as in influenza A.]

D. A. J. Tyrrell

Isachenko, V. A. **Comparative Investigations on A2 Influenza Virus Strains isolated in 1959 and 1957.** *Acta Virologica.* Prague. 1960, July, v. 4, No. 4, 250–54, 1 fig. [10 refs.]

A2 influenza virus strains isolated during an epidemic in 1959 reacted in HI tests with antisera to 1957 strains but antigenic differences were shown in cross HI tests with A2/59 antisera prepared in rats. Thus, some A2/59 strains did not react with the stock antigen A2/57-Singapore. Further, the author suggests that avidity and sensitivity to non-specific inhibitors should be considered as 2 distinct properties of a strain since 2 strains, one sensitive and the other insensitive to inhibitor, were both avid.

D. Taylor-Robinson

BERLIN, B. S. **Gross Physical Properties of Emulsified Influenza Virus Vaccines and the Adjuvant Response.** *J. Immunology.* 1960, July, v. 85, No. 1, 81–9. [24 refs.]

Influenza A virus (PR8), inactivated with formalin, was emulsified with petroleum oil and Arlacel A. The emulsions were inoculated into mice and the antibody response was estimated by haemagglutination inhibition. The viscosity of the emulsion was varied in several ways. Less viscous emulsions produced a better antibody response than more viscous emulsions. Other experiments suggested that emulsions with an intermediate degree of stability were better antigens than emulsions that were of relatively high or low stability. All the water-in-oil emulsions prepared showed an adjuvant effect when compared with unemulsified antigen.

D. A. J. Tyrrell

STAKHANOVA, V. M. **Antigenic Pattern of Type B Influenza Virus Strains isolated in 1959.** *Acta Virologica.* Prague. 1960, July, v. 4, No. 4, 246–9.

Lee, KRI (Moscow, 1949), BM8 (Leningrad, 1952) and B-55 (Moscow, 1955) strains of type B influenza virus and 7 other strains isolated in 1959 were used in cross HI tests with sera prepared in rats. All the 7 strains of virus isolated in 1959 had antigens in common with B-55 and BM8. However, only 2 strains (B/Moscow–Likh 5/59 and B/Krasnodar 106/59) had antigenic components in common with the KRI strain and none with the Lee strain of virus. *D. Taylor-Robinson*

GOTTSCHALK, A. & FAZEKAS DE ST. GROTH, S. **On the Relationship between the Indicator Profile and Prosthetic Group of Mucoproteins Inhibitory for Influenza Virus Haemagglutinin.** *J. General Microbiol.* 1960, June, v. 22, No. 3, 690–97, 1 fig. [24 refs.]

The haemagglutinins of 10 strains of influenza virus were converted to the indicator state and the inhibitory activity of 10 different mucoproteins was determined with each indicator virus. Some inhibitors were more active against some viruses than they were against others and the relative titres of each are presented as "indicator profiles". It was found that ovine submaxillary gland mucoprotein (OSM) and bovine submaxillary mucoprotein (BSM) both show a characteristic pattern in this "profile". The authors point out that chemical studies have recently shown that the prosthetic groups which react with influenza are the same chemically in both these substances; they suggest that the similar indicator profiles are a reflection of this chemical identity. Heat-stable serum mucoproteins of six species were found to have "profiles" similar to each other and different from OSM and BSM. *D. A. J. Tyrrell*

LINDENMANN, J. Interferon und inverse Interferenz. [**Interferon and Inverse Interference**] *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 146, No. 4, 287–309, 2 figs. [Numerous refs.]

No complement-fixing antibody to interferon could be found in 2 human influenza convalescent-phase sera, or in the sera of rabbits injected intramuscularly with interferon mixed with adjuvants. A method for titrating interferon in the presence of live influenza virus was developed, and it was possible to show by this means that the formation of interferon by the chorioallantoic membrane could be inhibited by infection with a sufficiently large dose of live virus before, at the same time as, or after treatment with inactivated virus. This phenomenon is referred to as "inverse interference".

D. J. Bauer

HANNOUN, C., PRUDHOMME, R. O. & GIUNTINI, J. Action des ultrasons sur les propriétés biologiques du virus de la grippe. [**The Action of Ultrasonic Vibration on the Biological Properties of Influenza Virus**] *Ann. Inst. Pasteur.* 1960, Aug., v. 99, No. 2, 188–201.

Very variable results have been reported following the treatment of influenza virus with ultrasonic vibrations. The present authors investigated the effect, on the results obtained with ultrasonic treatment, of purification of the virus, varying the time of treatment and adding 10% hydrogen to the gaseous phase. They used haemagglutination (HA), infectivity, complement fixation, antigenicity and electron microscopic appearances as measures of the effects of the treatments on the virus. The results are given in detail except for the electron micrographs which are to appear later.

The authors conclude that in the presence of hydrogen ultrasonic treatment dissociates aggregated particles and filaments, and then damages virus particles, causing an increase of HA and infectivity followed by a decline of infectivity. In the absence of hydrogen, especially when purified virus is used, there is a rapid destruction of infectivity and HA activity which they ascribe to oxidative processes.

[In the abstracter's opinion, the authors' claim that the antigenicity of a vaccine is increased by ultrasonic treatment would have been more convincing if it were supported by a full antigenic extinction titration.]

D. A. J. Tyrrell

NÁSZ, I. & TÓTH, Margaret. **Further Studies on the Cytopathogenic Effect of Adenoviruses in Human Amniotic Cell Cultures.** *Acta Microbiologica.* Budapest. 1960, v. 7, No. 2, 145–50, 12 figs. [14 refs.]

The authors studied the cytopathic changes to be seen in Giemsa-stained preparations of primary human amnion cultures which had been infected with the first 7 types of adenovirus. Most work was done with types 3 and 5 viruses. A notable feature was that type 3 virus caused cells to round up and shrink but they remained connected by protoplasmic threads whereas with type 5 virus the threads eventually broke down resulting in discrete degenerated cells. Nuclear granules remained diffuse in type 3 degeneration but aggregated into larger inclusions

in type 5 degeneration. (This is by no means a comprehensive study. Much fuller accounts of the cytopathic changes have been reported elsewhere, *e.g.* BOYER, *et al.* [this *Bulletin*, 1960, v. 35, 313].)

[See also this *Bulletin*, 1959, v. 34, 1191, *bis*.]

D. Taylor-Robinson

MORGAN, C.; GODMAN, G. C.; BREITENFELD, P. M.; ROSE, H. M. **A Correlative Study by Electron and Light Microscopy of the Development of Type 5 Adenovirus. I. Electron Microscopy** [MORGAN, GODMAN, BREITENFELD & ROSE]. *J. Exper. Med.* 1960, Aug. 1, v. 112, No. 2, 373–82, 30 figs. on 17 pls. [17 refs.] **II. Light Microscopy** [GODMAN, MORGAN, BREITENFELD & ROSE]. *Ibid.*, 383–402, 27 figs. on 5 pls. [52 refs.]

These papers present a readable and excellently illustrated account of a comprehensive study by means of electron microscopy and a wide range of histochemical techniques. About 12 hours after infection eosinophilic protein bodies appear in the nucleus of infected cells. Then virus particles develop in association with these bodies—they can be seen as basophilic material containing DNA in light microscopy. At about the same time a protein matrix, histochemically different from that in the eosinophilic bodies, forms in other parts of the nuclei and in this matrix protein crystals grow and seem to distort the nucleus. A crystal lattice can be seen in the crystals and this has a linear structure with a spacing of 400Å. There are also some data on the effect of various fixation procedures on the appearance of virus particles as seen with the electron microscope in sections of infected nuclei. The results are fully discussed and the papers should be read in full by all interested in any aspect of the subject. *D. A. J. Tyrrell*

HELLER, L. A. & SALENSTEDT, C. R. **One-Sided Immunologic Relation between Adenovirus and Infectious Canine Hepatitis Antigens.** *Virology.* New York. 1960, July, v. 11, No. 3, 640–45, 3 figs.

Fluids from tissue cultures infected with adenovirus (types 3, 4, 5 and 7) and the SBL-S-1 strain of infectious canine hepatitis (HCC) virus were used as antigens in complement-fixation (CF) tests. The titres for adenovirus antigen against 111 random human sera showed a close correlation with those for HCC antigen and the same sera. Paired sera from 10 patients with adenovirus type 7 infections showed rises in titre against either antigen. However, although 62 of the 112 dog sera fixed complement in the presence of HCC antigen, there was no fixation with the adenovirus antigens. Further, immunization of guineapigs with adenovirus types 1, 2, 5 and 6 produced sera which reacted to about the same titre with both adenovirus and HCC antigens but infection of guineapigs and puppies with HCC virus resulted in the appearance of CF antibodies against the HCC antigen only. This one-sided relationship was further demonstrated by gel diffusion precipitation. At least 3 heterologous lines, fusing with homologous lines, occurred between adenovirus serum and HCC antigen but no precipitate formed with HCC serum and adenovirus antigen. Finally, both antigens against adenovirus serum produced a fusion of lines and also a weak spur-like protrusion on the adenovirus side indicating a close similarity but not complete identity between the 2 antigens [this *Bulletin*, 1954, v. 29, 121].

The authors are not yet able to explain this one-sided relationship. *D. Taylor-Robinson*

SQUERI, L. & PERNICE, A. Osservazioni sulla specificità della reazione di emoagglutinazione tannico-indotta per gli adenovirus. [**On the Specificity of the Haemagglutination Reaction of Tanned Cells for Adenoviruses**] *Ann. Sclavo.* Siena. 1960, May–June, v. 2, No. 3, 225–34. English summary [8 lines].

In a previous paper (*Giorn. di Batteriol Virol. ed. Immunol.*, 1959, v. 52, 299) the authors showed the possibility of using tanned red cells for the study of adenovirus antibodies with antigens of adenovirus types, 1, 3, 5 and 9, a reaction which appeared to be group specific. They then discovered that tanned cells sensitized with culture fluid containing uninfected HeLa cells were equally agglutinated by rabbit immune serum. This prompted them to study the effect on sheep red cells of (1) HeLa maintenance medium free from cells, and (2) with cells; and (3) KB cells maintenance medium with cells, and (4) without cells. These sensitized cells were tested against immune serum produced in rabbits with adenovirus type 1, 3, 5 and 9. Cells treated with (1) and (2) reacted up to 1/2560, those treated with (4) up to 1/640, while those treated with (3) failed to react. A series of cross-agglutination experiments explained this as a specific reaction against horse or ox serum present in maintenance and in culture fluid for HeLa cells, as well as in the culture fluid for KB cells, by antibodies present in adenovirus immune sera. It also appeared that minimal traces of ox serum carried over on cells into maintenance fluid could produce antibodies *in vivo* and sensitization of red cells *in vitro*. Use of viral fluids free from any traces of serum, such as cells washed thrice in Earle saline solution, both in preparing immune serum and in sensitizing red cells, led to the production of sera completely type specific rather than group specific. HeLa cells cannot be used since these have to be kept and grown in serum media. Well washed KB cell viruses are satisfactory. *E. Agius*

PEREIRA, H. G. **A Virus Inhibitor produced in HeLa Cells infected with Adenovirus.** *Virology.* New York. 1960, July, v. 11, No. 3, 590–602, 3 figs. [28 refs.]

HeLa cells, infected with adenovirus type 5, were extracted with Arcton [this *Bulletin*, 1959, v. 34, 503] and the extract subjected to 3 cycles of centrifugation at 20,000 g for 90 minutes to remove virus particles. The final supernatant fluid was shown to contain a virus inhibitor as follows. The fluid was inoculated into HeLa cultures which were incubated for 18–20 hours at 37°. The cells were then washed and resuspended by sequestric

acid treatment. After low speed centrifugation the cells were resuspended in 5 ml. Gey's solution, counted (cells in excess of 2×10^6 per total volume discarded), washed again and the deposit challenged with adenovirus type 5, poliovirus type 1 or vaccinia virus at an in-put multiplicity of 100 ID per cell. After adsorption for 1 hour the cells were washed and transferred in 1 ml. amounts to 4 culture tubes and incubated for 44 hours (adenovirus) or 20 hours (polio and vaccinia viruses). The cultures were then used for complement-fixation (CF) and infectivity titrations. When the challenging virus was adenovirus type 5, a coverslip fragment placed in one of the cultures was examined by phase contrast after osmium fixation. In this way it was shown that pretreatment with inhibitor reduced the percentage of HeLa cells showing typical adenovirus lesions from 60–80% to 5%. Similarly, CF titres were reduced from 1 in 64–1 in 128 to 1 in 8 and infectivity titres by 95%. Inhibition of poliovirus and vaccinia virus multiplication was detected only by reduction of infective titres; an 8-fold and 5-fold reduction, respectively, in a representative experiment. As with the action of interferon, establishment of inhibition was gradual; it could be barely detected at 3 hours. Further, there was no inhibition 22 hours after removal of the inhibitor. Apart from adenovirus type 5, HeLa cells infected with types 1, 2, 4 and 6 also produced a substance showing inhibitory activity against adenovirus type 5; complement-fixing antigen (CFA) production and cytopathic effect were reduced to about 10% of the controls.

Adenovirus fractions A, B and C, isolated by chromatography on DEAE-cellulose columns [*ibid.*, 1960, v. 35, 513], were tested individually for inhibitory activity. This activity may be associated with the type-specific component common to B and C since they caused a reduction of CFA production to 23% and 27% of controls, respectively, whereas antigen A had no demonstrable activity. It was considered that the inhibitor acts by reducing the number of cells yielding virus; this was not due to interference with adsorption of poliovirus and probably not with adenovirus, although the error of titration was too large to make this certain. In these 2 respects the inhibitor was similar to interferon. However, it differed from interferon because it was neutralized by type-specific adenovirus antiserum, was not spontaneously liberated from cells and was completely destroyed by heating at 70° for 1 hour at *p*H 7·4.

D. Taylor-Robinson

GUERIN, L. F. & KITCHEN, S. F. **A Simple Tissue Culture Maintenance Medium utilizing Egg White.** *Proc. Soc. Exper. Biol. & Med.* 1960, July, v. 104, No. 3, 496–8.

5% egg albumin in physiological sodium chloride solution was found to be an effective and simple maintenance medium for primary monkey or rabbit kidney cells and for a human amnion and human kidney cell line. The medium was also successfully used for the growth of second generation monkey or rabbit kidney cells. The medium was also satisfactory with agar for overlaying infected cultures for plaque production. Egg albumin could not replace calf serum for the primary growth of monkey or rabbit kidney cells. The egg albumin did not inhibit enteroviruses and seemed to enhance the sensitivity of monkey kidney cells to enteroviruses in clinical specimens compared with those maintained in the routine fashion. The egg albumin was also inhibitory to some bacteria. It could be easily prepared and when reconstituted from the dried state remained equally effective.

A. J. Beale

TYNDALL, R. L. & LUDWIG, E. H. **Nutritional Requirements for the Production of Poliovirus Type II, Coxsackie B3, and Vaccinia Viruses by Continuous Animal Cell Cultures.** *J. Bacteriology.* 1960, July, v. 80, No. 1, 96–103, 12 figs. [11 refs.]

The nutritional requirements were determined for 4 continuous cell lines (HeLa, monkey heart, rabbit kidney and chick embryo vascular endothelium) for the production of 3 viruses (Coxsackie B3, poliovirus type 2 and vaccinia). The cells were washed thoroughly and starved in balanced saline (glucose-free) for 4–6 hours before use. In these experiments approximately 7×10^4 cells per tube were used with presumably about 1 ml. of medium. It was found that poliovirus type 2 was produced as well in cells maintained in balanced salt solution with glucose and glutamine as in medium 199. However, Coxsackie B3 and vaccinia required L-cystine for maximal production in all the cells though the effect was least marked for HeLa cells. Poliovirus production in monkey heart cells was also improved by L-cystine addition. L-cystine was the only essential amino acid in 199. As judged by Coxsackie B3 infection of monkey heart cells it was not required for virus adsorption. Similarly, in this system it could not be replaced by thioglycolate, ascorbic acid or glutathione.

A. J. Beale

ENDO, M., HAYASHIDA, T., MIZUNO, D. & TAKEMORI, E. Sur le développement du virus poliomyélitique dans un milieu simplifié du milieu synthétique No. 199. [**Propagation of Poliomyelitis Virus on a Simplified Modification of Medium 199**] *Japanese J. Exper. Med.* 1960, Feb., v. 30, No. 1, 89–93. [12 refs.]

It was found that a simple medium consisting of casein hydrolysate supplemented with glutamine, tryptophan, cysteine, sodium acetate and glutathione in Earle's solution was a satisfactory medium for the propagation of polioviruses in human amnion or monkey kidney cells. The yield of virus differed insignificantly from that obtained with medium 199 (MORGAN *et al.*, *Proc. Soc. Exper. Biol. & Med.*, 1950, v. 73, 1) and the same 3 strains of poliovirus, Mahoney type 1; MEF1 type 2; Saukett type 3.

A. J. Beale

YANG, Czau-Siung. **Studies on Poliovirus in Tissue Culture. II. Antibody Response and Virus Excretion in Taiwan Monkeys injected with Poliovirus.** *J. Formosan Med. Ass.* 1959, Oct. 28, v. 58, No. 10, 579–88, 4 figs. [14 refs.]

"1. Taiwan monkeys were inoculated with Type 1 (Mahoney), Type 2 (MEF_1), and Type 3 (Saukett) strains

of polioviruses and their neutralizing antibody titres and virus excretion in blood, throat and stools were tested in Hep-2 cells grown in Eagle's medium.

"2. The immune sera prepared were highly specific and so far as tested no normal neutralizing antibody was found.

"3. The monkeys were susceptible to intramuscular inoculation of Mahoney and MEF_1 strains of polioviruses. But re-inoculation of living virus to immunized monkeys could not cause paralysis even if the virus was detected in their blood and stools.

"4. After intramuscular inoculation of Mahoney strain (10^8 $TCID_{50}$/ml.), viremia was detected in one immunized and 2 non-immunized monkeys. The virus was also isolated from 2 throat swabs of non-immunized monkeys 4 days after the inoculation. The amount of polioviruses excreted in stools was small and also the period of virus excretion was short.

"5. Neutralizing antibody generally appeared 4 days after intramuscular inoculation of Mahoney strain (10^8 $TCID_{50}$/ml.). After re-inoculating the virus to immunized monkeys a negative phase of antibody content was remarkable in the monkeys immunized with Mahoney strain but not in those vaccinated with MEF_1 or Saukett strain."

MEDEARIS, D. N., Jr., ARNOLD, J. H. & ENDERS, J. F. **Survival of Polioviruses at Elevated Temperatures.** *Proc. Soc. Exper. Biol. & Med.* 1960, July, v. 104, No. 3, 419–23, 1 fig. 11 refs.]

Previous workers, most recently KAPLAN and MELNICK [this *Bulletin*, 1952, v. 27, 1147], have found that poliovirus is inactivated by 65°C. in 30 minutes. The present workers have found, however, that strains of all 3 types of poliovirus as tissue culture fluid (Medium 199 at approximately neutral *p*H) are not completely inactivated under these conditions. In very carefully controlled experiments they found that small quantities of type 2 virus survived 1 hour at 75°C. but not 1 hour at 85°C. Similarly, types 1 and 3 virus survived 1 hour at 65°C. but not at 75 or 85°C. The progeny of the rare heat-resistant variants were more heat-resistant than the stock cultures but less so than their parental strain. The survivors, after heating, produced cytopathic effects (CPE) in human amnion cells only after a much longer interval than usual. Thus the end point in a stock virus titration was reached in 6 days, whereas after heating to 55–65°C. the first appearance of CPE was delayed sometimes to between 21–35 days. The authors believe that the fact that they observed their cultures at intervals for 53 days is the most likely explanation for the difference between their results and those of others.

A. J. Beale

CABASSO, V. J., JUNGHERR, E. L., LEVINE, S., MOYER, A. W., ROCA-GARCIA, M. & COX, H. R. **Assessment of Correlation between certain *in vitro* Poliovirus Markers and Monkey Neurovirulence.** *Brit. Med. J.* 1960, July 16, 188–91, 1 diagram. [17 refs.]

Recently 3 *in vitro* markers for characterizing attenuated strains of poliovirus have been proposed. These are: t+, this character being the ability to grow at 40°C. as well as at 36°C.; d+, the ability to grow well under an agar overlay containing low amounts of bicarbonate; and MS+, the ability to grow well in a stable line of monkey kidney cells. The results of monkey neurovirulence tests on Lederle attenuated polio-vaccine strains show that after intracerebral inoculation (with high doses unspecified in the range 10^5 to over 10^7 TCD50) into monkeys, 8% of the animals were paralysed with the type 1 strain and 21% showed histological lesions (these figures exclude animals with only localized brain stem lesions). The figures for type 2 are 2% and 57% respectively and for type 3 6% and 16%. The *in vitro* marker characters were: type 1 d+ t− MS±; type 2 d± t− MS−; type 3 d+ t− MS+. Some experiments with the LSc attenuated derivative of the Mahoney strain of type 1 poliovirus were performed. This strain was isolated from single plaques, in monkey kidney cells, 4 times and found to be t− d− MS− and only caused localized lumbar cord lesions after a dose of $10^{7.5}$ TCD50 intramuscularly in 3 out of 4 animals and no lesions intracerebrally. A d+ t− MS− mutant derived from this strain caused lumbar cord lesions in 6 out of 12 animals inoculated intramuscularly and intracerebrally with $10^{7.5}$ or $10^{6.5}$ TCD50. A d+ t+ and a d− t+ mutant produced much more extensive histological lesions. The d− t+ strain paralysed 5 out of 8 animals given $10^{6.5}$ TCD50 intramuscularly or intracerebrally and the d+ t+ 8 out of 8 given $10^{7.5}$ TCD50 by the same routes. The authors note that there is not a clear-cut correlation between the *in vitro* markers and neuropathogenicity for monkeys and suggest that no method can replace the monkey neurovirulence test by the intracerebral route at present.

[It would seem that the monkey neurovirulence and probably the *in vitro* marker characters of the Lederle strains are unsatisfactory for a safe attenuated poliovaccine.] *A. J. Beale*

HUMMELER, K. & TUMILOWICZ, J. J. **Studies on the Complement-Fixing Antigens of Poliomyelitis. II. Preparation of Type-Specific Anti-N and Anti-H Indicator Sera.** *J. Immunology.* 1960, June, v. 84, No. 6, 630–34, 1 fig.

2 antigens of poliovirus have been distinguished. These are commonly called D for fully infectious virus and C for degraded D antigen [see LE BOUVIER, this *Bulletin*, 1960, v. 35, 316] after the zones of a sucrose density gradient [MAYER *et al.*, *ibid.*, 1958, v. 33, 1094]. In this paper the 2 antigens are called N for infectious virus and H for virus heated at 56°–60°C. The measurement of C. and D separately has proved difficult because of the presence of antibodies to both components in most poliovirus antisera. Mayer *et al.* [*loc. cit.*] have solved this problem by using the complement-fixation technique with specially selected monospecific anti-D and anti-C human sera. Unfortunately such sera are very rare and animal sera free of anti-C are difficult to obtain.

These authors have succeeded in obtaining such sera in guineapigs. Anti-H (or C) sera were obtained by

immunizing guineapigs with heated fluorocarbon-treated poliovirus (56°–60°). Anti-N (or D) sera were made by inoculation of guineapigs with high titre living virus treated with fluorocarbon. Occasional animals showed only an anti-N response but no consistent method of achieving this could be found. Therefore sera were absorbed with H virus antigen as follows. Sera were selected so that the anti-N titre was at least 1 in 64 and the anti-H titre not more than one-quarter of the anti-N. Such sera were mixed in equal volume with a 10-fold concentrate of H antigen and absorbed at room temperature for 2 hours and overnight +4°C. The viral antigen was then removed by ultracentrifugation and the procedure repeated once more. Such antisera proved satisfactory for measuring N antigen by complement fixation.

[Le Bouvier (*loc. cit.*) has solved the problem of the quantitative measurement of C and D antigens by diffusion through agar, using mixed anti-D and C sera. In this paper the terminology N for D and H for C is used because it has not yet been shown that all preparations that are serologically C sediment in a density gradient into the C zone characteristic of empty shells in the electron microscope.] *A. J. Beale*

Schmidt, Nathalie J., Lennette, E. H., Dennis, Juanita & Hagens, Shirley J. **The Behavior of Different Strains of Poliomyelitis Virus in the Complement Fixation Reaction. III. Comparison of the Potency of Complement Fixing Antigens derived from Different Strains of Poliomyelitis Virus.** *J. Immunology.* 1960, July, v. 85, No. 1, 67–71.

The authors have previously shown that there is very little difference in the ability of complement-fixing antigens derived from different strains of the 3 types of poliovirus to detect type specific antibodies in human sera [this *Bulletin*, 1959, v. 34, 398; 1960, v. 35, 713]. They now report studies on variations of antigen titre of poliovirus preparations as HeLa cell tissue culture fluid, using antisera against Mahoney type 1, MEF1 type 2 and Saukett type 3 strains of poliovirus. It was found that there were no significant differences between 7 strains of type 2 and 112 of type 3 and in particular the Sabin attenuated strains proved very satisfactory. However, in the study of 17 type 1 strains it appeared that the attenuated LSc strain was definitely a less potent antigen. Also the LSc strain was not tested in the trials of sensitivity in detecting type 1 antibodies. However, it seems likely that perfectly satisfactory CF antigens for all 3 types can be made from Sabin's attenuated strains although, as the authors point out, it remains to be shown that the strains have not reverted to virulence during the passage in HeLa cells necessary to prepare the antigens. *A. J. Beale*

Crawford, J. G. & Field, M. F. **Potency of Poliomyelitis Vaccines estimated by an Antibody Combining Test.** *J. Bacteriology.* 1960, July, v. 80, No. 1, 111–18, 3 figs. [15 refs.]

The multiplicity of potency testing methods for poliovaccine is eloquent testimony to the inadequacy of all of them. A favoured *in vitro* method has been the antibody combining power test (for a recent account see Benyesh-Melnick and Melnick, this *Bulletin*, 1960, v. 35, 92) and this paper describes a modification designed to reduce the variability of the test. 50-fold vaccine concentrates prepared by Baron's method [*ibid.*, 1958, v. 33, 1092] were used in serial 2-fold dilutions against serial dilutions of a specific antiserum (containing 0, 1, 2, etc., units of antibody—1 unit being contained in the 50% end point dilution against 100 TCD50 of virus) each in 1 ml. After 5 hours at 35°C. and overnight at +4°C. the tubes were challenged with 100 TCD50 of virus and incubated in the same way before being inoculated into roller tubes to detect virus. The 50% end point of vaccine combining with antiserum (AC50) was calculated for each serum dilution used. These were plotted against the units of antiserum. The antibody combining power of the vaccine was arbitrarily defined as the serum unitage value where the plot of AC50 intercepted the base line at an AC50 of $\log_2 3$. The method, although cumbersome, appeared to be a reproducible technique for measuring a quality of poliovaccine related to monkey potency. A nomogram was constructed relating monkey potency to antibody combining value.

[The full technical details are given.] *A. J. Beale*

Dostal, V., Gädeke, R., Grünewald, H., Mauler, R., Mittelstrass, H. K. & Sauthoff, R. Untersuchungen über den intracellulären Nachweis des Echo-Virus Typ 9 in Affennieren-Kulturzellen. [**Investigations on the Intracellular Detection of Type 9 ECHO Virus in Monkey Kidney Cell Cultures**] *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 146, No. 4, 367–84, 8 figs. [43 refs.]

The development of type 9 ECHO virus in monkey kidney cell cultures has been studied by means of fluorescence and electron microscopy. 4 hours after infection abnormalities were observed in the mitochondria, which were enlarged and structureless. Vacuolated areas were present in the cytoplasm which were considered to be the remains of mitochondria, and also cystic areas containing osmiophilic granules 30 mμ in diameter. In preparations treated with fluorescent antibody faint fluorescence was seen at the periphery of the cell 1–3 hours after infection, becoming more intense after 6 hours, with the appearance of clumps of fluorescent material. No fluorescence could be observed in the nuclei. Infective virus could be detected in the cells after 3 hours, and reached a maximum titre 8 hours after infection. *D. J. Bauer*

Ellem, K. A. O. & Colter, J. S. **The Interaction of Infectious Ribonucleic Acid with a Mammalian Cell Line. I. Relationship between the Osmotic Pressure of the Medium and the Production of Infectious Centers.** *Virology.* New York. 1960, June, v. 11, No. 2, 434–43, 1 fig. [12 refs.]

Mengo encephalomyelitis virus was grown in L strain mouse fibroblasts. Mengo RNA was prepared by phenol extraction and salting out with NaCl. Its infectivity was titrated either by plating on L cell monolayers or by

incubating a mixture of RNA and L cells in suspension, then diluting and plating the cells on L cell monolayers to determine the number of infected cells. Irregular results were obtained and the infectivity was unstable when RNA in 0·14 M phosphate buffered saline (PBS) was plated directly: when the NaCl was increased to 0·8 M the number of plaques was inversely proportional to the dilution. L cells were, however, damaged by the hypertonic saline. This difficulty did not arise when cell suspensions were infected. With this system and NaCl molarities from 0·14 to 0·87 M the number of plaques (indicating infected cells) increased from 13 at 0·14 M to 270 at 0·67 M and diminished to 23 at 0·87 M. When sucrose concentrations were used the maximum number of plaques was found at 0·7 M. Both these optimal concentrations are at about the same osmotic pressure, 4·0–4·1 times that of physiological saline. 1·5–2·0 times as many plaques were found at the optimal sucrose concentration as at the optimal NaCl concentration.

When intact Mengo virus was allowed to interact with a cell suspension, and free virus was then neutralized with gamma globulin, concentrations of NaCl greater than physiological prevented infection from occurring. A similar but much less marked effect was seen with sucrose. This was shown to be due probably to failure of adsorption of virus to cells.

Hypertonic solutions appear to modify cells so that they are more receptive to RNA but not to intact virus. They may increase the stability of RNA perhaps by inhibiting ribonuclease. Another possibility is that they prevent immobilization of RNA by cytoplasmic proteins.

C. E. Gordon Smith

PORTERFIELD, J. S. & ROWE, C. E. **Hemagglutination with Arthropod-Borne Viruses and its Inhibition by Certain Phospholipids.** *Virology*. New York. 1960, Aug., v. 11, No. 4, 765–70.

Haemagglutinins were prepared from 4 group A and 8 group B arthropod-borne viruses by Arcton 63 extraction of mouse brain suspensions in *p*H 9·0 borate-saline [this *Bulletin*, 1959, v. 34, 400] followed by centrifugation at 10,000 r.p.m. for 1 hour. 6 of these antigens were tested against crude α– and β– lipoprotein extracts from human serum, and against a crude human red blood cell phospholipid extract. High titres of inhibition were obtained with all against 5 group B but not against a group A antigen. Dengue type 2 (Tr. 1751) appeared to be a sensitive indicator and it was tested against 12 purified human blood cell fractions. All ethanolamine- and serine-containing phospholipids were inactive. All 3 active fractions contained choline and one of them was mainly sphingomyelin. Choline chloride was found inactive but lecithin from hens' eggs was found to be a potent inhibitor. Sphingomyelin from ox brain was tried but it agglutinated goose cells and was inactive at dilutions where it did not. Egg lecithin lost its inhibitory activity after incubation with *Clostridium perfringens* [*welchii*] α toxin (lecithinase). All the active materials had about the same activity in terms of moles of phosphate (minimum concentrations of $13-38\times10^{-10}$) except egg lecithin which had about 0·5% of this activity. Purified lecithin was inactive.

The inhibitors of group B but not group A arthropod-borne viruses appear to be choline-containing phospholipids related to lecithin. *C. E. Gordon Smith*

OSTERRIETH, P.; BLANES-RIDAURA, G.; DELEPLANQUE-LIÈGEOIS, P.; RENOIRTE, R. Recherches sur le virus Chikungunya au Congo belge. I. Isolement du virus dans le Haut-Uélé [OSTERRIETH & BLANES-RIDAURA]. [**Studies on Chikungunya Virus in the Congo. I. Isolation of the Virus in Upper Uélé Region**] *Ann. Soc. Belge de Méd. Trop.* 1960, Feb. 29, v. 40, No. 1, 199–203. II. Enquête sérologique [OSTERRIETH, DELEPLANQUE-LIÈGEOIS & RENOIRTE]. [**II. Serological Survey**] *Ibid.*, 205–13, 2 maps.

I. 3 patients were studied near Doruma in the Eastern Province of the Congo. They were aged 13, 25 and 28 years. All had fever and severe headache, other symptoms were backache, abdominal discomfort, diarrhoea, and a scarlatiniform rash. One had slight neck rigidity. All recovered within a week but sequelae included weakness, headache and pains in the limbs. Chikungunya virus or a very closely related virus was isolated from the blood of all 3 by inoculation of 3-day-old mice. 2 patients were shown to have developed neutralizing antibody to the virus during the course of the illness by an intracerebral test in 3-day-old mice.

II. Human sera were collected in 2 areas of the Eastern Province: 92 from Doruma and 50 from each of 3 villages around Basoko. Doruma is on a plateau which is a mosaic of cultivated land and savannah forest with numerous water-courses lined by gallery forest in which monkeys are numerous. The inhabitants are farmers and hunters. Of the 3 Basoko villages, 1 was in a large area of plantations, 1 in a small area of cultivation surrounded by secondary forest, and 1 on the river close to swamp forest.

The sera were tested undiluted against 100 LD50 of Chikungunya virus (Entebbe strain) in a suckling-mouse intracerebral neutralization test. In Doruma the incidence of antibody rose from 1 out of 9 (11%) under the age of 10, to 21 out of 67 (31%) over 20 years of age. In the Basoko villages no antibody was found in children under 10 and in only 1 village (swamp forest) in children between 10 and 20 years of age (3 of 10). The incidence in adults reached 30–60% in the last 2 villages but reached 30% only in those over 40 years of age in the area of large plantations.

2 groups of sera from chimpanzees were also tested. One group was from savannah forest in Ango and Bondo (in the Doruma region) in which 1 of 9 were positive at an estimated age of under 1 year, 4 of 27 aged 1–5 years and 2 of 9 older animals. The second group was from forest around Stanleyville: 2 of 6 aged under 1 year, 3 of 23 aged 1–5 and 0 of 5 older animals had antibody.

The authors consider that these results are probably specific but mention the possibility of cross-reaction with the related Semliki Forest virus. The results suggest that Chikungunya virus is endemic over large areas of the Congo and that it has a forest reservoir. There appears to have been an epidemic recently in the Doruma area.

C. E. Gordon Smith

THOMAS, L. A., KENNEDY, R. C. & EKLUND, C. M. **Isolation of a Virus closely related to Powassan Virus from** *Dermacentor andersoni* **collected along North Cache La Poudre River, Colo.** *Proc. Soc. Exper. Biol. & Med.* 1960, June, v. 104, No. 2, 355–9.

A pool of 20 *Dermacentor andersoni* collected in Colorado in 1952 was inoculated into 4-day-old mice. A blind passage was made after 7 days but between the 8th and 13th days the remainder of the mice sickened and died. The blind passage mice were sick after 5 days and this incubation period remained with passage. Re-isolation was unsuccessful. A haemagglutin was prepared which was active from *p*H 6·0 to 7·0 and at temperatures from 4°–37°C. The maximum haemagglutinin titre was at *p*H 6·8 and 22°C. In inhibition tests against antisera to 4 group A, 10 group B arthropod-borne viruses and 8 other viruses reaction was found only with group B agents. In a complement-fixation test against group B antisera (Powassan, St. Louis, Japanese B, Ilheus, Murray Valley, West Nile, Uganda S, Zika, Ntaya, yellow fever) strong cross-reaction was found only with Powassan virus [this *Bulletin*, 1960, v. 35, 717, *bis*.] In cross-neutralization tests Powassan and the new virus were clearly identical or closely related. Russian spring-summer antiserum neutralized the new agent as strongly as Powassan antiserum but antiserum to the new agent neutralized Russian spring-summer virus only in an intraperitoneal (not an intracerebral) neutralization test.

C. E. Gordon Smith

MÁLKOVÁ, Doubravka. **Virus and Antibodies in the Lymph and Blood of Sheep infected experimentally with the Virus of Tick-Borne Encephalitis.** [Correspondence.] *Nature.* 1960, Aug. 20, v. 187, 716.

Following on previous work in mice [this *Bulletin*, 1960, v. 35, 829] experiments were made in sheep so that lymph and blood samples could be collected. Lymph was collected from the cannulated thoracic duct, blood from a branch of the contralateral jugular vein. Virus was inoculated subcutaneously. When $3–4 \times 10^9$ intracerebral mouse LD50 were given in the metatarsus of a hind limb, virus was detected 60 minutes later in the lymph. Virus did not appear to enter the blood stream except through the thoracic duct. 7 and 12 days after infection, re-infection caused no virus to appear in either blood or lymph. Neutralizing antibody was detected earlier and in higher titre (up to the 7th day) in the lymph than in blood. When the thoracic duct was exteriorized so that virus did not pass [from it] into the blood, antibody was also found in the lymph. [This is a preliminary report without experimental details.]

C. E. Gordon Smith

SCHMIDT, J. R., SCHMIDT, M. L. & MCWILLIAMS, J. G. **Isolation of Phlebotomus Fever Virus from** *Phlebotomus papatasi*. *Amer. J. Trop. Med. & Hyg.* 1960, July, v. 9, No. 4, 450–54.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 1260.]

BURGDORFER, W. & LACKMAN, D. **Identification of the Virus of Colorado Tick Fever in Mouse Tissues by means of Fluorescent Antibodies.** *J. Bacteriology.* 1960, July, v. 80, No. 1, 131–6, 4 figs. [11 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 1260.]

MCINTOSH, B. M., KOKERNOT, R. H. & PATERSON, H. E. **Witwatersrand Virus: an Apparently New Virus isolated from Culicine Mosquitoes.** *South African J. Med. Sci.* 1960, Apr., v. 25, No. 1, 33–7. [14 refs.]

In April 1958 an outbreak of febrile illness occurred at Germiston, near Johannesburg and collections of mosquitoes coming to bite man were made in that area. A pool of *Culex rubinotus* were inoculated into 2-day and adult mice. The suckling mice were sick or dead on the 4th/5th days, and adults between the 9th and 16th days. Passage and re-isolation were successful. On passage the incubation period in suckling mice was 2–3 days and in adults 6–7 days. The brain and blood of sick suckling mice titrated in sucklings was 7·5 and 7·7 log respectively. Guineapigs were unaffected by 9500 mouse LD50 but developed antibody.

The virus passed a gradocol filter of 275mμ APD and was sensitive to sodium desoxycholate. It was successfully lyophilized. A haemagglutinin with optimum titre at *p*H 6·0 was prepared by sucrose-acetone extraction of suckling mouse brain and by acetone-ether extraction of suckling mouse serum. No cross-reaction in haemagglutinin-inhibition tests was found with antisera to a selection of 25 arthropod-borne viruses although the homologous antiserum titred 2560. The homologous antiserum similarly gave negative results with antigens of 13 arthropod-borne viruses. Complement-fixation tests with a sucrose-acetone brain antigen revealed no cross-reaction with antisera to 17 arthropod-borne viruses. The virus was not significantly neutralized by antisera to 31 viruses. Witwatersrand virus is therefore provisionally classified as a new arthropod-borne virus.

2 convalescent sera from the febrile outbreak had no Witwatersrand antibody. Of survey human sera, antibody was found in 0 of 118 from the South African highveld, 0 of 42 (7 inconclusive) from Northern Natal, 3 of 30 (6 inconclusive) from Namacurra in Portuguese East Africa, and 0 of 49 from 2 other areas in Portuguese East Africa.

C. E. Gordon Smith

IMMUNITY

ZIMMERMANN, G. Passive Mäuseschutzversuche mit Human-γ-Globulinen verschieden alter Kontrollnummern und verschiedener Herstellung. [**Observations on the Passive Protection of Mice with Human Gamma Globulin varying in Age and in Method of Preparation**] *Schweiz. med. Woch.* 1960, July 23, v. 90, No. 30, 801–7. [13 refs.]

The globulin which is prepared at Dessau on a large scale from serum obtained from the healthy placenta was given to the mice in the following doses: 0·5 ml. intraperitoneally (i.p.) 18 hours before infection, 0·25 ml. intravenously (i.v), at the same time and 0·25 ml. i.v. 2 hours after infection. Comparison was made with controls and with batches of mice treated with sulphanilamide or antibiotics. The chemotherapeutic agents were given as follows: 2 hours after infection 0·5 ml. i.p. and 0·5 ml. i.v.; 6 hours and 22 hours later 0·5 ml. i.v.; 0·9% solution of sulphanilamide and 0·1% solution of antibiotics were the concentrations of solutions commonly used. Infection was with a dilution of a 24-hour serum broth culture and 0·5 ml. was given i.p. Infections with streptococcus, staphylococcus and *Escherichia coli* were studied.

Survivals in the mice protected with gamma globulin varied from 30% to 100% at the end of the experiments and exceeded those obtained with sulphanilamide, human serum or horse serum. They were usually equal to and sometimes exceeded those obtained with streptomycin or tetracycline. *J. W. McLeod*

LEON, M. A., with the technical assistance of A. RANSBY. **The Reaction between Dextrans and the Properdin-Complement System. I. Inhibition by Excess Dextran.** *J. Immunology.* 1960, Aug., v. 85, No. 2, 190–96, 8 figs. [18 refs.]

LEE, L. & STETSON, C. A., Jr. **Studies on the Mechanism of the Shwartzman Phenomenon. Accelerated Cutaneous Reactivity to Bacterial Endotoxins.** *J. Exper. Med.* 1960, June 1, v. 111, No. 6, 761–72, 1 fig. on pl. & 2 text figs.

Intradermal injections of bacterial endotoxins in normal rabbits ordinarily result in delayed inflammatory reactions which are not visible for several hours and reach maximum development only after a day or two. Such reactions resemble in many respects those of delayed hypersensitivity [this *Bulletin*, 1955, v. 30, 1033]. This paper records the observation that this dermal reactivity of rabbits to bacterial endotoxins can be modified and accelerated by previous intravenous injection of the endotoxins. In rabbits so treated the reaction became visible within one hour, and approached maximum intensity in 6 hours, at which time no inflammatory reaction was visible in the control animals. This accelerated reaction differed from that in the control animals by resembling the Arthus reaction, showing pronounced oedema and acute inflammatory changes; it also had a longer duration. Although the reaction was apparently specific for endotoxins as a group, specificity did not extend to individual endotoxins; *i.e.*, rabbits which received a modifying injection of one endotoxin responded with typical accelerated reactions to skin testing with other endotoxins.

It was possible in 6 of 9 experiments passively to transfer the accelerated reaction with serum, and this appeared to be related to the presence of non-precipitating cross-reactive antibody, rather than to specific precipitating antibody. *D. A. Cannon*

INDERBITZIN, T. Allergie und Immunität. [**Allergy and Immunity**] *Schweiz. med. Woch.* 1960, Sept. 10, v. 90, No. 37, 1027–30.

Book Reviews

GRUNDY, Fred [M.D., M.R.C.P., D.P.H.]. **Preventive Medicine and Public Health. An Introduction for Students and Practitioners.** 4th Edition. pp. viii + 316, illustrated. 1960. London: H. K. Lewis & Co. Ltd., P.O. Box 66, 136, Gower Street, W.C.1. [27s. 6d.]

The fact that this 4th edition has been called for within 3 years of the last [see this *Bulletin*, 1958, v. 33, 421] and 9 years from the first is a striking testimonial to its value. It is fortunate that Professor Grundy has been able to finish it before his departure from the chair of Preventive Medicine in the University of Wales for the even busier life which awaits him as an Assistant Director-General of the World Health Organization at Geneva.

It is a good and well-written book: not big enough to frighten the medical undergraduate or practitioner yet sufficiently comprehensive to give them adequate information about what preventive medicine and public health stand for. It will, also, serve to orientate those preparing for, or who have already begun, a career in public health.

The book begins with a dissertation on the precise meanings of Epidemiology, Social Medicine, Preventive Medicine and Public Health with their interlocking relationship.

New material includes the Local Government Act 1958, the Mental Health Act 1959, the Cranbrook Report on the Maternity Services and recent developments in the production of morbidity statistics. Even so, important new medical discoveries are now made so frequently,

and in public health the emphasis on what should receive priority changes so quickly, that, as in books on the diagnosis and treatment of disease, those on public health are apt to be out of date while they are going through the press. Nevertheless this book deals accurately and fully with the scene as it was at the time it was written and moreover has an important chapter on history which will not need to be altered with the passing years.

The book is warmly recommended and, no doubt, yet another edition will appear before very long.

Allen Daley

AMERICAN PUB. HEALTH ASS. **Control of Communicable Diseases in Man.** An Official Report of the American Public Health Association. 9th Edition. 234 pp. 1960. New York 19: 1790 Broadway, N.Y. London: H.M. Stationery Office. [7s. 6d.]

This most valuable small book is revised every 5 years. [For earlier reviews see this *Bulletin*, 1945, v. 20, 368 and 1956, v. 31, 478.] The new edition retains the same method of presentation but the number of disease headings has increased from 118 to 134. Some sections have been expanded and this is particularly true of that dealing with the arthropod-borne viral infections where an excellent account is given of the ever increasing number recognized in man. The primary object of the book is to provide the data required for an enlightened control of communicable diseases and in this it eminently succeeds.

Most of the criticisms made by the reviewer in 1956 [*loc. cit.*] have been met but herpes zoster still only receives a passing reference under chickenpox and *Plasmodium falciparum* malaria could be differentiated, both in its manifestations and in its lack of a persistent exo-erythrocytic phase, more clearly from the other varieties of malaria. Cerebral cysticercosis is stated to be a chronic disease with a relatively high fatality, the word "relatively" replacing "ultimately" of the 8th edition. [The patient previously quoted by the reviewer as surviving to 81 years is now aged 86.] Maduramycosis is only referred to under nocardiosis. It perhaps deserves separate treatment but classification is difficult as fungi of different genera may produce similar or totally different clinical diseases.

The notes on specific treatment do little more than indicate if chemotherapy is available, and this primarily as an aid to control. Thus their detailed examination is scarcely called for, but the masking of *Trypanosoma rhodesiense* infections by prophylactic pentamidine is again not mentioned and the methods of treatment of amoebiasis and schistosomiasis are still somewhat at variance with British practice. As is to be expected, the usual abbreviations in spelling, adopted in America, prevail but the etymologically correct spelling of loiasis now used by this *Bulletin* might replace "loaiasis" in the next edition.

Great care has been taken in preparing the book and the publishers have taken the unusual step of providing a "Revised and Corrected Index" supplied loose, to replace that printed in the 9th edition, as the original index did not reach the high standard desired by the Chairman of the Committee responsible for the book.

This small volume can be confidently recommended to all practitioners of public health and curative medicine.

Frederick J. Wright

TOP, Franklin H. [A.B., M.D., M.P.H., F.A.C.P., F.A.A.P., F.A.P.H.A.] & Collaborators. **Communicable and Infectious Diseases. Diagnosis, Prevention, Treatment.** 4th Edition. 812 pp., 122 figs. & 15 coloured pls. 1960. St. Louis: The C.V. Mosby Co. London: Henry Kimpton, 134, Great Portland Street, W.1. [£7. 10. 0.]

This considerable volume of 812 pages is a text-book of diseases of infections which are encountered in the United States. The principal author has obtained the collaboration of 21 colleagues, among whom appear very few names which will be recognized by readers in Britain.

The preliminary 8 chapters include an outstanding review of chemotherapeutic and antibiotic agents but also chapters on infection and immunity, and the management of communicable diseases which contain much very banal material. The glossary of medical terms appended at the end appears superfluous if the book is designed for medical readers.

The system of classification used is by the portal of entry of infection, which results in some odd juxtapositions an example of which, in a section entitled Mucous Membrane or Skin, is the sequence anthrax, cat-scratch fever, hookworm disease, the leptospiroses, tetanus and tularaemia.

The production is handsome, the print clear and the illustrations, many of which are in colour, are of a high order—even in the X-ray reproductions the lesions are nearly always recognisable which is quite unusual in the common run of text-books.

In general, the outlook of this work is parochial, and it is remarkable how little attention has been paid to research and experience published outside the United States. It is also inevitable in such a co-operation that the standard of authorship should be uneven; much is high, a proportion outstanding—the reviewer would specially commend the chapters dealing with streptococcal, staphylococcal and tuberculous diseases—but one contribution is unworthy of inclusion, namely, that on malaria.

Viral diseases receive detailed and up-to-date treatment, and the book includes good descriptions of poliomyelitis, Coxsackie, ECHO and adenovirus infections. Nevertheless, the first omits mention of the important advances made in Scandinavia in the treatment of bulbar paresis by tracheotomy and positive pressure respiration, nor does it give information on the intense endemicity of poliovirus infections throughout the juvenile populations of the tropical belt. The chapter on rabies also omits mention of the myelitic form of the disease which is characteristic of infection transmitted by vampire bats.

It will surprise the English reader to discover that, in the United States, 1 person in 6 of the population has been infected with *Trichinella spiralis*, though in the majority few symptoms arise. Trichinosis appears to be

a national disease attributable to the hamburger, which frequently contains ill-cooked pork of doubtful origin.

An otherwise excellent chapter on typhoid fever makes no mention of the urinary carrier. The 5 principal venereal diseases are well described but no account of the non-gonococcal forms of urethritis is given, though, as in Europe, these are in the ascendant in the U.S.A. while gonorrhoea declines.

Further examples of the limited outlook of this book which will strike the reader in Britain are the omission of reference to the great volume of research on leprosy carried out in past and present in India and in West Africa, to the important publications by the Amoebiasis Research Unit in Durban, South Africa, and to many English publications on the management of tetanus by chlorpromazine sedation, by curarization and by prolonged anaesthesia.

It is, however, the chapter on malaria which the informed reader will find most wanting. The brief historical review, while mentioning Laveran's discoveries and the earliest description by MacCallum in the United States of exflagellation of the male gametocyte, dismisses such names as Manson and Ross, Bignami, Grassi and Bastianelli in the comprehensive phrase "the British and Italian workers". An astonishing error in regard to human malaria is made in the following sentence:—"Following the bite of an infected mosquito the parasites undergo 6 to 8 days' development in some of the fixed tissue cells, principally in the spleen and bone marrow, before they appear in the blood stream." Quinacrine (Atabrine) is described as "a synthetic drug, discovered at the close of World War II", whereas this drug (atebrin or mepacrine are its pseudonyms in Britain) has been in wide use since the early 1930's and protected many thousands of allied fighting men from 1943 onwards. The special action of the 8-amino-quinolines on the exo-erythrocytic phases of *P. vivax, P. malariae* and *P. ovale* infections is not explained and the indication for the use of these important drugs is not therefore made clear.

A review cannot avoid criticism but let it be said of this book that the very good and the good by far out-balance the bad, but its orientation is towards the United States in subject matter and outlook. *J. H. Walters*

Wallis, H. R. E. **Brucellosis in England.** With a preface by H. J. Harris. 140 pp., 9 figs. 1959. London: A. S. O'Connor & Co. Ltd. [25s.]

The author is a paediatrician practising in a centre of rural England. This monograph gives in Chapter 4 the case reports of 35 patients where the diagnosis of brucellosis was confidently made. All the patients were children or adolescents. These are very readable accounts and are intended to alert practitioners to the possible occurrence of brucellosis in its protean and often indefinite clinical manifestations. As autochthonous human infections in Britain (where the species has been identified) have always been proved to be due to *Brucella abortus* the author assumes that all his patients acquired the infection from cattle (mostly from unpasteurized milk) with the exception of one where the disease was considered to have been congenital, although the diagnosis was not made until the age of 6 years.

In no case was *Brucella* isolated and the author criticizes those who limit their records to patients in whom cultural confirmation has been obtained, suggesting that such a criterion distorts the picture of brucellosis as it commonly occurs in Britain. The author's clinical descriptions are typical of brucellosis, for the most part of a mild type, but the incidence of cervical adenitis appears to be greater in his group of patients than in series composed chiefly of adults, see Conway [this *Bulletin*, 1950, v. 25, 34]. He is fully aware that not every reader will be convinced that the diagnosis was always established either in the 35 cases where it is claimed to have been confirmed or in the 7 additional cases presented as probable. 15 of the 35 "proved" cases yielded a negative serum when the agglutinins were first determined and in a further 6 were positive only in a dilution less than 1 in 60. The author rightly accepts a positive brucellin skin test as evidence only of exposure to the disease but where this is followed by the appearance or increase of agglutinins, or where the patient responds to antibiotics, he is inclined to accept the diagnosis as established. Cases are presented in which the diagnosis was formerly thought to have been abdominal tuberculous lymphadenitis.

The first 3 chapters give a general survey and will be useful to those unacquainted with brucellosis but as the literature quoted frequently refers to infections by *Br. melitensis,* in countries other than Britain, the quotations are not always fully appropriate to the subject.

The author states that blood culture is "rarely positive in *abortus* infections". It is true that in Britain a disappointingly small percentage of cases are culturally confirmed. The reasons for this are not altogether clear. Certainly the strain of *Br. abortus* prevalent in Central and East Africa is frequently cultured in both acute and chronic infections. In treatment the author favours a tetracycline orally plus a mixture of streptomycin and dihydrostreptomycin intramuscularly. In a footnote on page 40 he refers to the use of novobiocin as advocated by Torres Gost [*ibid.*, 1958, v. 33, 341] but not to the unpleasant side effects and failures from this antibiotic (see Reig and López, *Lancet*, 1959, v. ii, 972).

[An attractive book with a laudable aim, but somewhat uncritical.] *Frederick J. Wright*

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